Supplementary Appendix

Supplement to: Anderson EJ, Creech CB, Berthaud V, et al. Evaluation of mRNA-1273 vaccine in children 6 months to 5 years of age. N Engl J Med. DOI: 10.1056/NEJMoa2209367

This appendix has been provided by the authors to give readers additional information about the work.

Supplementary Appendix

Table of Contents

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Supplementary Methods

Trial Oversight

The trial is being conducted in 79 US and 8 Canadian sites in accordance with the International Council for Technical Requirements for Registration of Pharmaceuticals for Human Use, Good Clinical Practice Guidance, and applicable government regulations. The central Institutional Review Board (Advarra) approved the protocol and consent forms. All participants provided written informed consent.

Moderna, Inc. was responsible for trial design (in collaboration with the Biomedical Advanced Research and Development Authority [BARDA], NIAID, Coronavirus Vaccine Prevention Network, and study co-chairs), site selection and monitoring, and data analysis. Investigators were responsible for data collection. Authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol. EJA, SSG and JET drafted the manuscript, and all authors provided approval.

Study Eligibility Criteria

Inclusion criteria

Participants were eligible to be included in the study (in age group 6 months-5 years) only if all the following criteria applied:

1. Participants were male or female, 6 months-5 years of age at the time of consent/assent (screening visit), in good general health, in the opinion of the investigator, based on review of medical history and screening physical examination.
2. If the participant had a chronic disease (eg, asthma, diabetes mellitus, cystic fibrosis, human immunodeficiency virus [HIV] infection), the disease should be stable, per investigator assessment, so that the participant can be considered eligible for inclusion. Stable diseases were those which had no change in status or in the medications required to control them in the 6 months prior to screening visit. Note: a change in medication for dose optimization (eg, insulin dose changes), change within class of medication, or reduction in dose were not considered signs of instability.
3. In the investigator's opinion, the parent(s)/ Legally Acceptable Representative (LARs) understood and were willing and physically able to comply with protocol-mandated follow-up, including all procedures, and provided written informed consent and participants were willing to provide assent.
4. Participants 2 years or older had a body mass index at or above the third percentile according to WHO Child Growth Standards at the screening visit.
5. The participant was born at full-term (≥37 weeks' gestation) with a minimum birth weight of 2.5 kg.

Exclusion criteria

Participants were excluded from the study if any of the following criteria apply:

1. Had a known history of SARS-CoV-2 infection within 2 weeks prior to administration of IP or known close contact with anyone with laboratory confirmed SARS-CoV-2 infection or Covid-19 within 2 weeks prior to administration of IP.
2. Was acutely ill or febrile 24 hours prior to or at the screening visit. Fever was defined as a body temperature ≥38.0°C/≥100.4°F. Participants who met this criterion could have visits rescheduled within the relevant study visit windows. Afebrile participants with minor illnesses were enrolled at the discretion of the investigator.

3. Had previously been administered an investigational or approved CoV (eg, SARS-CoV-2, SARS-CoV, Middle East respiratory syndrome-CoV) vaccine.
4. Had undergone treatment with investigational or approved agents for prophylaxis against Covid-19 (eg, receipt of SARS-CoV-2 monoclonal antibodies) within 6 months of enrollment.
5. Had a known hypersensitivity to a component of the vaccine or its excipients. Hypersensitivity included, but was not limited to, anaphylaxis or immediate allergic reaction of any severity to a previous dose of messenger RNA Covid-19 vaccine or any of its components (including polyethylene glycol [PEG] or immediate allergic reaction of any severity to polysorbate).
6. Had a medical or psychiatric condition that, according to the investigator's judgment, may pose additional risk because of participation, interfere with safety assessments, or interfere with interpretation of results.
7. Had a history of a diagnosis or condition that, in the judgment of the investigator, may affect study endpoint assessment or compromise participant safety, specifically the following:

- Congenital or acquired immunodeficiency, excluding HIV infection, as described in Inclusion Criteria 2
- Chronic hepatitis or suspected active hepatitis
- A bleeding disorder that was considered a contraindication to IM injection or phlebotomy
- Dermatologic conditions that could affect local solicited AR assessments
- Any prior diagnosis of malignancy (excluding nonmelanoma skin cancer)

8. Had received the following:

- Any routine vaccination with inactivated or live vaccine(s) within 14 days of the first vaccination or plans to receive such a vaccine through 14 days following the last study vaccination.
- Influenza vaccine could be given, however, not within 14 days of or following Dose 1 or Dose 2. If a participant received an influenza vaccine, this was captured within the concomitant medication electronic case report form
- Systemic immunosuppressants or immune-modifying drugs for >14 days in total within 6 months of the day of enrollment (for corticosteroids, ≥1 mg/kg/day or ≥10 mg/day prednisone equivalent, if participant weighed >10 kg). Participants could have visits rescheduled for enrollment if they no longer met this criterion within the screening visit window. Inhaled, nasal, and topical steroids were allowed.
- Intravenous or subcutaneous blood products (red cells, platelets, immunoglobulins) within 3 months of enrollment.

9. Had participated in an interventional clinical study within 28 days prior to the screening visit or planned to do so while participating in this study.
10. Was an immediate family member, or household contact, of an employee of the study site or Moderna or someone otherwise directly involved with the conduct of the study. As applicable, family members/household contacts of employees of the larger institution or affiliated private practice not part of the study site were enrolled.

Randomization and Blinding

In Part 2, up to 4000 participants each in the 6–11years, 2–5 years, and 6–23 months age groups were randomized in a 3:1 ratio to the mRNA-1273 arm (n=≤3,000 participants in each group) or placebo arm (n=≤1000 participants in each group). Random assignment of participants in part 2

of the study uses a centralized interactive response technology, in accordance with pre-generated randomization schedules.

The part 1 open-label phase comprised dose-escalation and age de-escalation to select the preferred dose for each age group based on safety, tolerability, and immunogenicity results (Figure S1, and online protocol). In part 1, children 2−5 years were enrolled at the planned initial mRNA-1273 dose of 50-µg. Dose-escalation to 100-µg dose was not initiated based on Internal Safety Team (IST) review of solicited adverse reactions (ARs) post-injection 1 of 50-µg in this age group, and solicited ARs observed after administration of 100 µg dose in the previously reported older age group (6-11 years).[1] Assessment of the 50-µg dose (n=150 enrolled) in the 2−5 year group indicated a rate of fever similar to that observed after the 100 µg dose in the older age group (6-11 years). Accordingly, the protocol was modified to assess a lower dose (25-µg) in a group of 2−5-year-old children in part 1, a dose that proved less reactogenic than 2 injections of 50-µg of mRNA-1273. The youngest children (6−23 months) received 25-µg of mRNA-1273 in part 1 and the tolerability profile of 25-µg was considered acceptable. No children were enrolled in the 50-µg mRNA-1273 study arm in children 6−23 months per IST recommendation.

As part 1 of this study was open-label, blinding procedures were not applicable. Part 2 was conducted in an observer-blind manner until emergency use authorization made all participants eligible for unblinding. Until the unblinding trigger, the investigator, study staff, study participants, study site monitors, and Sponsor personnel (or its designees) were blinded to the study vaccine administered, except a limited number of pharmacy personnel, accountable for preparing and administering, managing and documentation of mRNA-1273 (or placebo) to all participants and have no other study functions. Access to the randomization code was strictly controlled at the pharmacy, and study vaccine was prepared in a secure location not accessible or visible to other study staff. An opaque sleeve over the syringe was used for injection to maintain the blind at the time of injection. Unblinded study site monitors, not involved in other aspects of monitoring, were assigned as study vaccine accountability monitors to ensure that study sites follow all proper accountability, preparation, and administration procedures. An unblinded statistical and programming team performed the primary analyses in part 2 and pre-specified sponsor team members were unblinded to the primary analysis results.

Trial Vaccine

The mRNA-1273 vaccine is a lipid nanoparticle dispersion of an mRNA that encodes the prefusion stabilized S protein of SARS CoV-2 formulated and composed of 4 lipids as previously described.[2] The mRNA-1273 injection is provided as a sterile liquid at a concentration of 0.2 mg/mL in 20 mM Tris buffer containing 87 mg/mL sucrose and 4.3 mM sodium acetate at pH 7.5, consisting of 25-µg, 50-µg or 100-µg doses of mRNA1273, or place-bo (normal saline) per assigned treatment diluted with normal saline to a final injection volume of 0.5 mL. Each participant is to receive 2 intramuscular injections of study vaccine approximately 28 days apart (days 1 and 29) for parts 1 and 2, administered into the deltoid muscle or anterolateral thigh (per investigator's discretion). At each visit after study vaccine is administered, participants are monitored for a minimum of 30 minutes, and assessed for body temperature measurements (oral preferred for participants >4 years of age, tympanic preferred for participants ≤4 years of age, but other methods acceptable in context of Covid-19 precautions) and monitoring for local or systemic reactions. The study sites are appropriately

staffed with individuals with basic cardiopulmonary resuscitation training/certification. Either on-site resuscitation equipment and personnel or appropriate protocols for the rapid transport of participants to a resuscitation area or facility are required.

Study Outcomes

Primary objectives included the evaluation of the safety and reactogenicity of up to 3 dose levels (25, 50, and 100 µg) of mRNA-1273 vaccine administered as 2 injections, 28 days apart in 3 age groups and to infer the efficacy of mRNA-1273 (25, 50, and 100 µg), administered as 2 injections 28 days apart based on the noninferiority of serum antibody geometric mean concentrations and seroresponse rates compared with young adults (18-25-years). Secondary objectives included evaluation of the incidences of Covid-19, SARS CoV-2 infection regardless of symptoms, and asymptomatic SARS-CoV-2 infection after vaccination with mRNA 1273 or placebo. Covid-19 is defined as clinical symptoms consistent with Covid-19 AND positive RT-PCR for SARS-CoV-2.

Safety Assessment

Safety and reactogenicity are assessed by clinical review of all relevant parameters including solicited adverse reactions (ARs) both local and systemic, unsolicited adverse events (AEs), serious AEs (SAEs), medically-attended AEs (MAAEs), AEs of special interest (AESIs), AEs leading to withdrawal from study vaccine and/or study participation, and physical examination findings. Solicited ARs and unsolicited AEs are coded by system organ class (SOC) and preferred term (PT) according to the Medical Dictionary for Regulatory Activities (MedDRA). Two modified versions of The Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventative Vaccine Clinical Trials (DHHS 2007) are used in this study for solicited ARs including the pediatric toxicity scale used for children older than 36 months, and the infant/toddler toxicity scale used for children 6 to 36 months of age, inclusive.[3]
All safety analyses are based on the Safety Set, except summaries of solicited ARs which are based on the Solicited Safety Set. All safety analyses are provided by age and vaccination group unless otherwise specified.

Solicited Adverse Reactions

The eDiary is used to solicit daily participant reporting of ARs using a structured checklist. Participant's parent(s)/ Legally Acceptable Representative (LARs) recorded such occurrences in an eDiary on the day of each dose of injection and for the 6 days after the day of dosing. Severity grading of reactogenicity occurred automatically based on participant entry into the eDiary according to the toxicity grading scales, modified from the Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventative Vaccine Clinical Trials (DHHS 2007). If a solicited local or systemic AR continues beyond day 7 after vaccination, the participant's parent(s)/LAR(s) was prompted to capture details of the solicited local or systemic AR in the eDiary until resolved or the next study vaccine injection occurred, whichever occurred first. Capture of details of ARs in the eDiary did not exceed 28 days after each vaccination. Adverse reactions recorded in the eDiary beyond day 7 were reviewed by the study site staff either during the next scheduled telephone call or at the next study site visit. All solicited ARs (local and systemic) are considered related to the study vaccine.

eDiaries

At the time of consent, participants' parent(s)/ Legally Acceptable Representative (LARs) confirmed their willingness to complete an eDiary, and prior to enrollment on Day 1, were instructed to download the eDiary application or were provided eDiary devices. At the injection visits, parents and LARs were instructed (day 1) or reminded (day 29) on oral or tympanic thermometer usage to measure body temperature, ruler usage to measure injection site erythema and swelling/induration (hardness), and assessment of localized axillary swelling or tenderness on the same side as the injection arm/thigh and recorded data under the supervision of study site staff and retrained as necessary, and to continue recording data into the eDiary on the day of injection and for 6 days afterwards.

Information recorded includes solicited local and systemic reactogenicity ARs, that occur on the day of each vaccine administration and during the 7 days afterwards per specific instructions (any ARs recorded in the eDiary beyond day 7 are reviewed by the study site staff either during the next scheduled telephone call or at the next study site visit), daily oral or tympanic body temperature measurement performed at approximately the same time each day using the thermometer provided by the study site, measurement of solicited local ARs (injection site erythema and swelling/induration) sizes using the ruler provided by the study site, and any medications taken to treat or prevent pain or fever on a day of injection or for the next 6 days.

The eDiary is the only source document allowed for solicited systemic or local ARs (including body temperature measurements). Electronic diaries were specifically designed for this study by the Sponsor and included prelisted solicited ARs and intensity scales and also a blank space for the recording of information on other AEs (unsolicited AEs) and concomitant medications/vaccinations. Participants' parent(s)/LAR(s) were instructed to complete eDiary entries daily and had a limited window on the following day to complete assessments for the previous day. Study site staff reviewed eDiary data with participants' parent(s)/LAR(s) at telemedicine visits 7 days after each injection.

Completion of eDiary questionnaires are alternated every two weeks with safety telephone calls to capture the occurrence of AEs, MAAEs, SAEs, AESI, or AEs leading to withdrawal. The eDiary is used every 4 weeks, starting at day 71 through 183 and again starting at day 223 through day 363 and prompted the participant's parent(s)/LAR(s) to complete an eDiary questionnaire that collects the following data:

- Changes in health since last completing the questionnaire or since in contact with the study site
- Any MAAEs, AESIs, or SAEs
- Known close contact with someone in the household who has known Covid-19 or SARS-CoV-2 infection. Per the CDC, "close contact" to someone with Covid-19 is defined as follows:
    - Being within 6 feet for a total of 15 minutes or more
    - Providing care at home
    - Having direct physical contact (hugged or kissed them)
    - Sharing eating or drinking utensils
    - Being sneezed or coughed upon or getting respiratory droplets on the participant
- Any experience of symptoms of Covid-19

Safety calls are conducted to discuss participants' health and review their eDiary and take place at day 85 through 197 and again from day 237 through 377. Any new safety information reported during safety telephone calls or at study site visits (days 1, 29, 30, 43, 57, 209 and 394) including

solicited reactions not already captured in the eDiary are described in the source documents as a verbally reported event and described as a solicited event and entered on the solicited AR eCRF. Grade 3 or higher systemic ARs reported in eDiary by the parents/LARs were reviewed by the sites during safety calls to verify the accuracy of grading and duration of event. As grade 3 and grade 4 events lasting longer than 24 hrs contribute to pause rule thresholds, sites called parents to verify all grade 3 or higher fevers entries and durations per pause rule assessment. Three of the reported 40 degree Centigrade temperatures were thus found to have been entered in error (ie the child had no fever). However, eDiary entries could not be corrected once entered. If an eDiary record resulted in identification of relevant safety events according to the study period or of symptoms of Covid-19 or exposure, a follow-up safety telephone call was triggered.

The investigator is responsible for the documentation of AEs regardless of treatment group or suspected causal relationship to study vaccine. For all AEs, the investigator pursued and obtained information adequate to determine the AE outcome and to assess whether the AE met criteria for classification as an SAE, requiring immediate notification to the Sponsor or its designated representative. Care is taken not to introduce bias when detecting AEs and/or SAEs, using open-ended and nonleading verbal questioning of the participant and participant's parent(s)/LAR(s) to inquire about the occurrence of an AE. After the initial AE/SAE report, the investigator is required to proactively follow each participant at subsequent visits and contacts. All AEs and SAEs were to be treated as medically appropriate and followed until resolution, stabilization, until the event was otherwise explained, or the participant was lost to follow-up.

Immunogenicity Assessment

Neutralizing antibody titers are measured with the use of validated pseudovirus neutralizing antibody assays as described below. In part 1, geometric mean titer (GMT) was assessed using the validated lentivirus pseudovirus (D614G) assay at 50% (ID50) and 80% (ID80) inhibitory concentrations (Duke University). In part 2, geometric mean concentrations (GMC) are assessed using a reporter virus microneutralization assay shown to be concordant with the Duke assay. Binding antibody levels were also assessed using the Meso Scale Discovery (MSD) binding antibody assay in parts 1 and 2.

Per-protocol Immunogenicity Subset

The primary analysis population for immunogenicity is the Per-protocol Immunogenicity Subset, unless specified otherwise. The Per-protocol Immunogenicity Subsets of both the KidCOVE cohorts and the young-adult (18-25 year) COVE cohort consisted of subsets of participants in the full analysis set selected for immunogenicity sampling and testing. The PP Immunogenicity Subset included participants selected for the Immunogenicity Subset who received planned doses of study vaccine per schedule, complied with the immunogenicity testing schedule, and had no major protocol deviations (ie excluded participants who did not receive the 2nd injection or discontinued the study before day 57, and in KidCOVE those [majority of enrolled participants, enrolled after Cohorts A, B and C enrollment] who did not have blood sample collection scheduled at day 57 [ie missing immunogenicity data at day 57]) that would impact key or critical data. Participants who were RT-PCR positive or seropositive at baseline were excluded from the Per-protocol Immunogenicity Subset, in addition to participants with HIV who were receiving highly active anti-retroviral therapy (HAART) which can interfere with the

pseudovirus assay.[4] The Per-protocol Immunogenicity Subset was used for all analyses of immunogenicity unless specified otherwise.

Immunogenicity Assays

Part 1 Pseudovirus neutralization assay

Neutralizing antibodies to SARS-CoV-2 in serum samples from trial participants were measured using a validated SARS-CoV-2 Spike (S)-Pseudotyped Virus Neutralization Assay in 293/ACE2 cells, adopted from an assay developed by Drs. Barney Graham and Kizzmekia Corbett at the Vaccine Research Center, NIH.[5,6] The assay was optimized, qualified, and validated by the "Neutralizing Antibody Core" Laboratory at Duke University for evaluation of neutralizing antibody activity after vaccination. Quantification of SARS-CoV-2 neutralizing antibodies utilized lentivirus particles expressing SARS-CoV-2 S protein (Wuhan-Hu-1 isolate including D614G) on their surface and containing a firefly luciferase (Luc) reporter gene for quantitative measurements of infection by relative luminescence units (RLU) in transduced 293T cells expressing high levels of ACE2 (293T/ACE2 cells). Virus was applied to the cells with or without pre-incubation with antibodies; neutralizing antibodies reduced infection, resulting in lower RLUs. Serial dilution of antibodies was used to produce a dose-response curve. Neutralization was measured as the serum dilution at which RLU was reduced by 50% (ID_{50}) and 80% (ID_{80}) relative to mean RLU in virus control wells (cells + virus but no sample) after subtraction of mean RLU in cell control wells (cells only).

Part 2 Pseudovirus neutralization assay

Post-vaccination serology samples from participants ages 6 months through 5 years (part 2) and from a comparator group of 18-25-year-olds were tested using a validated reporter virus microneutralization assay (PPD, part of Thermo Fisher Scientific Vaccines Laboratory Services, Richmond, Virginia).[7,8] This cell-based assay measures the SARS CoV-2 neutralizing antibody inhibition of the infection of 293T-ACE2 cells by SARS CoV-2 reporter virus particles (RVP; Wuhan-Hu-1 isolate including D614G). The serum antibody concentration is determined by interpolating the mean of the replicate foci forming unit values from the fitted reference standard curve calibrated to the first WHO International Antibody Standard for SARS CoV-2 Lot 20/136. The interpolated antibody concentrations were dilution corrected, and the final concentration is the antibody concentration associated with the lowest dilution with an antibody concentration within the quantifiable range of the assay. The results are reported as final antibody GMC in AU/mL.

Meso Scale Discovery (MSD) binding antibody assay

The validated Meso Scale Discovery (MSD, Rockville, MD) assay (SARSCOV2S2P [VAC123]; was used for the detection of binding antibody against variants.[9] The assay uses an indirect, quantitative, electrochemiluminescence method to detect SARS-CoV-2 binding IgG antibodies that bind to the SARS-CoV-2 full-length spike protein (Wuhan-Hu-1 ancestral SARS-CoV-2; beta [B.1.351] with the following amino acid changes in the spike protein [L18F, D80A, D215G, Δ242-244, R246I, K417N, E484K, N501Y, D614G, and A701V]; delta [B.1.617.2; AY.4; Alt Seq 2] with the following amino acid changes in the spike protein [T19R, T95I, G142D, Δ156/157, R158G, L452R, T478K, D614G, P681R, and D950N]); omicron [B.1.1.529; BA.1]

with the following amino acid changes in the spike protein [A67V, ΔH69-V70, T95I, G142D, Δ143-145, Δ211/L212I, ins214EPE, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, and L981F]) in human serum. The assay was performed by PPD Vaccine Laboratory, Wilmington, NC and is based on MSD technology which employs capture molecule MULTI-SPOT® microtiter plates fitted with a series of electrodes.

Assessment of Incidence of SARS-CoV-2 Infection and Covid-19

The incidence rates of Covid-19 (symptomatic SARS-CoV-2 infection), SARS-CoV-2 infections (asymptomatic or symptomatic infections), and asymptomatic SARS-CoV-2 infections were assessed as secondary endpoints. To be considered as a case of Covid-19 for the evaluation of the efficacy endpoint, the participant must have at least 1 nasal swab (or respiratory sample, if hospitalized) positive for SARS-CoV-2 by RT-PCR AND one of the following: fever (temperature ≥ 38ºC/≥100.4ºF) or chills (of any duration, including ≤ 48 hours); shortness of breath or difficulty breathing (of any duration, including ≤ 48 hours); cough (of any duration, including ≤ 48 hours); fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; abdominal pain; nausea or vomiting; diarrhea; poor appetite/poor feeding for at least 48 hrs.

Covid-19 cases were assessed for efficacy by two methods based on each of two definitions. This included the **CDC case definition** which requires at least 1 prespecified clinical systemic symptom (fever [temperature> 38ºC/≥ 100.4ºF] or chills [of any duration, including ≤ 48 hours], cough [of any duration, including ≤ 48 hours], shortness of breath or difficulty breathing [of any duration, including ≤ 48 hours], fatigue, headache, myalgia, nasal congestion or rhinorrhea, new loss of taste or smell, sore throat, abdominal pain, diarrhea, nausea or vomiting, poor appetite or poor feeding), OR at least ONE of the following respiratory signs/symptoms (cough [of any duration, including ≤ 48 hours], shortness of breath or difficulty breathing [of any duration, including ≤48 hours]), AND at least one positive RT-PCR test for SARS-CoV-2. The second method for efficacy assessment was based on the **primary case definition used in the pivotal phase 3 COVE study** in adults requiring either at least TWO of the following systemic symptoms (Fever [≥ 38ºC/≥ 100.4ºF], chills, myalgia, headache, sore throat, new olfactory and taste disorder(s), OR the participant must have experienced at least ONE of the following respiratory signs/symptoms (cough, shortness of breath or difficulty breathing, OR clinical or radiographical evidence of pneumonia) AND at least one positive RT-PCR test for SARS CoV-2. Use of the COVE case definition allowed alignment of Covid-19 case assessment with that in the COVE study, and the CDC case definition, defined by a single symptom, was amenable to the assessment of Covid-19 to children, who typically present with milder clinical symptoms than adults.

A formal approach was used to surveil Covid-19 cases and identify SARS-CoV-2 infections (regardless of symptoms). Surveillance for symptoms consistent with Covid-19 was conducted via telephone calls or eDiary prompts starting at enrollment and performed biweekly through day 71 and monthly thereafter. During the study, participants who experienced potential symptoms of Covid-19 were asked to arrange an unscheduled illness visit at the study site. At the illness visit, participants were assessed clinically and a SARS-CoV-2 RT-PCR test (nasal swab) was administered. A SARS-CoV-2 or Covid-19 Symptom Assessment in the eCRF was

completed for every participant with relevant clinical symptoms assessed at any study visit (ie, scheduled or unscheduled illness visit), or if symptoms were described during a safety call.

Routine assessment for SARS-CoV-2 infection (regardless of symptoms) is assessed by performing RT-PCR testing on pre-planned nasal swab samples collected on days 1, 29 (day of injection), 43 (if visit is applicable), 57 (1 month after injection 2), 209 (6 months after injection 2), and 394 (12 months after injection 2). Of note, asymptomatic SARS-CoV-2 infection is most often identified via samples obtained at prespecified, scheduled study visits from either nasal swab samples (RT-PCR) or serum samples (bAb levels against SARS-CoV-2 nucleocapsid as measured by Roche Elecsys) and is also identified at unscheduled study visits triggered by potential exposure, with no subsequent development of clinical symptoms (regardless of being unscheduled or illness visits). In addition, serum samples collected in a subset of participants at prespecified time points for measurement of vaccine-induced immunogenicity (variable time points based on subcohort) were also tested for the presence of Ab against non-vaccine (SARS-CoV-2 nucleocapsid) to also identify prior, asymptomatic infection.

Statistical Methods

The planned sample size in part 1 was ~750 participants (~375 participants at each dose level of mRNA-1273) in the initial 6–11-year age group, there is at least a 90% probability to observe at least 1 participant with an AE at a true AE rate of 1% for a given dose level. In each of the younger age groups (2−5 years and 6−23 months), safety assessment occurred during the conduct of part 2 after approximately 375 participants have been exposed to mRNA-1273 at the dose level selected for part 2. The planned sample size in part 2 of the study was considered to be sufficient to support a safety database in the pediatric participants 6 months to <12 years of age. With up to 3,000 participants each in the 6-11 years, 2−5 years, and 6−23 months age groups exposed to mRNA-1273 at a given dose level in part 2, the study had at least a 95% probability to observe at least 1 participant with an AE at a true 0.1% AE rate for a given dose level.

A subset of Full Analysis Set (FAS) participants (Immunogenicity Subset) in each age group was selected for measuring immunogenicity data. The immunogenicity samples of the Immunogenicity Subset were processed, and the analysis of primary immunogenicity endpoint was based on the PP Immunogenicity Subset.

- As an acceptable antibody threshold of protection against Covid-19 is not available at the time of analysis for the primary immunogenicity endpoint, noninferiority tests of the 2 null hypotheses based on the 2 coprimary endpoints were performed. The sample size calculation for each of the 2 noninferiority tests was performed, and the larger sample size was chosen for the study.
- With approximately 289 participants receiving mRNA 1273 in the PP Immunogenicity Subset of each age group and young adults (18-25 years of age) in the COVE study, there will be 90% power to demonstrate noninferiority of the immune response, as measured by the antibody GM value in children at a 2-sided alpha of 0.05, compared with that in young adults (18-25 years) receiving mRNA-1273, assuming an underlying GMR value of 1, a noninferiority margin of 0.67 (or 1.5), and a point estimate minimum threshold of 0.8. The standard deviation of the natural log-transformed levels is assumed to be 1.5.
- With approximately 289 participants receiving mRNA 1273 in the PP Immunogenicity Subset of each age group and young adults (18 - 25 years of age) in COVE, there will be at least 90% power to demonstrate noninferiority of the immune response as measured by SRR in children at a 2-sided alpha of 0.05, compared with that in young adults (18-25 years)

receiving mRNA-1273, assuming SRR of 85% in young adults (18-25 years), true SRR of 85% in children (or true rate difference is 0 compared to young adults), a noninferiority margin of 10% and a point estimate minimum threshold of -5% in SRR difference.

- For this study, if the true seroresponse rates were assumed to be 95% or higher in both the young adults 18-25 years from COVE and an age group in children, with between-group true difference within 4%, there would be a >90% power to demonstrate noninferiority by seroresponse rates in children compared with young adults, at a 2-sided alpha of 0.05.
- Assuming approximately 25% of participants in the Immunogenicity Subset in part 2 would not meet the criteria to be included in the PP Immunogenicity Subset, approximately 528 participants in part 2 (~396 receiving mRNA-1273 and ~132 receiving placebo) will be selected for the Immunogenicity Subset from which approximately 289 participants on mRNA-1273 will be suitable for the PP Immunogenicity Subset in part 2.

Noninferiority was assessed by an analysis of covariance model conducted using Ab at day 57 in log-scale as the dependent variable and a group variable (pediatric age group in KidCOVE versus young adults [18-25 years of age] in COVE) as the fixed variable. The GM values of the pediatric age group at day 57 were estimated by the geometric least square mean (GLSM) from the model, and the GMR (ratio of GM values) was estimated by the ratio of GLSM from the model with corresponding 2-sided 95% CI to assess the difference in immune response for the pediatric age group (2−5 years and 6−23 months of age, KidCOVE) compared with the young adults (18-25 years of age) in COVE at day 57. The noninferiority of GM in the 2−5 years and 6−23 months age groups was demonstrated if the lower bound of the 95% CI of the GMR was ≥0.67 based on a noninferiority margin of 1.5. In addition, the GMR point estimate ≥0.8 (minimum threshold) was required for the success criteria of the immunogenicity objective based on GMT. The GMR with 95% CI calculated using t-distribution was provided to assess if the 2 methods were consistent in the analysis results.

The number and percentage of participants with seroresponses due to vaccination is provided with 2-sided 95% CI using the Clopper-Pearson method at each postbaseline time point, with day 57 being of the primary interest. The seroresponse rate difference with 95% CI using the Miettinen-Nurminen (score) confidence limits at day 57 was provided between children receiving mRNA-1273 in KidCOVE and the young adult (18-25 years) group receiving mRNA-1273 in COVE. The noninferiority of seroresponse rate in the 6−23 month and 2−5 years groups was considered demonstrated if the lower bound of the 95% CI of the seroresponse rate difference is ≥-10% based on the noninferiority margin of 10% and the seroresponse rate difference point estimate ≥-5% (minimum threshold).

For evaluation of the secondary endpoints, incidences of symptomatic and asymptomatic Covid-19, and SARS-CoV-2 infection, the number and percentage of participants who had an event are provided. The incidence rate was calculated as the number of cases divided by the total person-time. The 95% CI of the incidence rate was calculated using the exact method (Poisson distribution) and adjusted by person-time. Person-time is defined in Part 2 as the total time from randomization date to the date of event, last date of study participation, censoring time, or efficacy data cut-off date, whichever is earliest. Vaccine efficacy was estimated defined as 1 minus the ratio of incidence rate (mRNA-1273 vs. placebo) and the 95% CI of the ratio is calculated using the exact method conditional upon the total number of cases, adjusting for person-time.

Safety was assessed in the safety set, except for solicited ARs, which were evaluated in the solicited safety set. Safety results are provided by treatment group and by age group. Safety and reactogenicity were assessed by clinical review of all relevant parameters including solicited local and systemic ARs, unsolicited AEs, SAEs, MAAEs, AESIs, AEs leading to discontinuation, and physical examination findings. The number and percentage of participants with any solicited local and systemic ARs, and with any solicited ARs during the 7-day follow-up period after each injection by toxicity grade are provided. A 2-sided 95% exact CI using the Clopper-Pearson method is provided for the percentage of participants with any solicited AR. The number and percentage of participants with unsolicited AEs, SAEs, MAAEs, severe AEs, and AEs leading to discontinuation from IP or withdrawal from the study are summarized.

Unsolicited AEs are presented by MedDRA preferred term and system organ class. The number of events of solicited ARs, unsolicited AEs/SAEs, and MAAEs are reported in summary tables accordingly. For all other safety parameters, descriptive summary statistics are provided. An ad-hoc evaluation was performed to compare reactogenicity in children (2−5 years and 6−23 months) versus young adults (18-25 years) from the COVE trial.[10]

Part 1 Results

Safety

2−5 year cohort

At the time of the data cutoff date, the median duration days (interquartile range [IQR]) of follow-up from part 1 in children 2−5 years of age was 236 (224-238) days for the 25-µg group and 266 (204-307) days for the 50-µg group after injection 1 and 207 (189-210) days for the 25-µg group and 237 (173-274) days for the 50-µg group after injection 2. The overall incidence of solicited local and systemic adverse reactions (ARs) after any injection was higher in the 50-µg than in the 25µg group and were mainly grade 1 or 2 (Tables S5-S7). Grade 3 systemic ARs were reported in a lower proportion of participants in the 25-µg group (1.4%), compared to the 50-µg group (9.7%). No grade 4 solicited systemic ARs were reported in part 1 in the 25-µg group; a single grade 4 solicited systemic AR (fever >40°C) was reported in the 50-µg group. The mean duration of solicited ARs was 1-2 days (Table S9).

Overall, unsolicited AEs up to 28 days after any injection including unrelated and related AEs and MAAEs were more frequently reported in the 50-µg group (56/155; 36.1%) compared to the 25-µg group (16/69; 23.2%). There were no severe unsolicited AEs reported in the 25-µg group (**Error! Reference source not found.**). As of the data cutoff date, no participant in either group was discontinued from the study due to an AE in part 1. There were no SAEs, no deaths, no cases of MIS-C or other AESIs, and no cases of myocarditis or pericarditis in either treatment group reported at the time of the data cutoff date. While the safety profile of the 25- and 50-µg groups were similar, the 25-µg dose was considered better tolerated on the basis of the reactogenicity profile where both systemic and local ARs occurred with less frequency and severity in the 25-µg group compared to the 50-µg group after any dose, and was selected for evaluation in the randomized, placebo-controlled part 2 of the study. The Data Safety and Monitoring Board (DSMB) concurred with the choice of the 25-µg dose.

6−23 months

The median duration of follow-up was 263 days (interquartile range [IQR] 258- 266) after injection 1 and 233.5 days (IQR 228.0-238.0) after injection 2. Because of the unfavorable

reactogenicity profile seen in the older age group (2-<6 years) with the 50-µg dose, only the 25-µg dose was evaluated in this age group (6 months to <2 years), per the internal safety team recommendation. The majority of solicited ARs after any injection were grade 1 (64/150; 42.7%) or grade 2 (70/150; 46.7%), and no grade 4 events were observed (Table S8). The mean duration of solicited ARs was 3 days (Table S10).

Unsolicited AEs were reported in greater than 1% of participants for part 1 (Table S11). Overall, AEs were typical for this infant/toddler population and for post-vaccination events. Four (2.7%) participants experienced 6 severe AEs reported within 28 days of any dose, including decreased appetite (2 [1.3%]), febrile convulsion (1 [0.7%], this AE was also reported as an SAE, not related, with a concurrent viral illness), cough (1 [0.7%]), wheezing (1 [0.7%]), and urticaria (1 [0.7%]) The last 3 events occurred in one participant 21 days after dose 2 and were assessed as not related by the investigator. No participants in the 6–23-month-olds in part 1 were discontinued from the study due to an AE. Two participants (2/150; 1.3%) experienced SAEs within 28 days after vaccination; neither was considered to be related to treatment. No deaths, no cases of MIS-C, and no cases of myocarditis or pericarditis were reported as of the data cut off.

Immunogenicity

2−5 year cohort

At day 57 (28 days post-dose 2) 2−5-year-old part 1 children who received 25-µg (n=50) mRNA-1273 had nAb GMT of 1013.8 (846.2-1214.5) with 100% achieving seroresponse (Table S12). Comparison of this GMT to that of young adults in (18-25 years; n = 295) yielded a GMR (95% confidence interval [CI]) of 0.78 (95% CI 0.61-1.00) and a difference in seroresponse rates (SRR) of 1.0% (95% CI -6.1%- 3.0%). Part 1 2−5-year-old recipients of 50-µg (n=69) mRNA-1273 had nAb GMTs of 1844.1 (1602.336, 2122.404) with 100% achieving seroresponse. Comparison of this GMT to that of the young adults yielded a GMR of 1.42 (95% CI, 1.14-1.77) and a difference in SRR of 1.0% (95% CI, -4.3%, 3.0%).

6−23 months

At day 57 (28 days after dose 2), 25-µg mRNA-1273 elicited nAb GMT (95% CI) of 1782.6 (1542.0-2060.7) in children 6−23 months and 100% met the definition of seroresponse (Table S13). Comparison of nAb GMT from children 6−23 months receiving 25-µg (n = 98) to young adults (18-25 years; n = 295) receiving 100-µg 1299.9 (1170.6-1443.4) yielded a GMR of 1.4 (95% CI, 1.12-1.67). The difference in seroresponse rates at day 57 between the 2 groups was 1.0% (95% CI, -2.8%-3.0%).

Part 2 Fever Analysis Results

Fever was reported in both treatment groups, after any injection, with a higher proportion in the mRNA-1273 group after injection 2. Graphical representation of the percentage of participants reporting maximum fevers with temperatures of 38-38.4ºC, 38.5 to 38.9°C, 39 to 40°C, or >40°C after each injection is provided in (Figure S5). The majority of the reported fevers were in the range of ≥38 to 38.9°C with only rare cases of fever >40°C after either injection in both treatment groups. Reported fevers lasted for a median duration of 1 day after any injection in both treatment groups. In the mRNA-1273 group, fever was most commonly reported on day 1 or day 2 after vaccination. For the remaining days after day 2 for either injection, the reported fever rates were similar between the mRNA-1273 and the placebo groups (Figure S6), and lower

than on day 1 and day 2, reflecting the short duration of the fevers occurring after each injection. There were 13 fever events >40°C reported: 11 (0.4%) participants in the mRNA-1273 and 2 (0.2%) in the placebo groups. As per protocol, any AR reported as a grade 3 or 4 event prompted an investigator inquiry to ensure these events did not fulfil a study pause rule; therefore, further description of grade 4 fever events is available. Investigator inquiry of these reported 13 grade 4 (> 40°C) fever events determined that 3 of the 13 fever events were incorrectly reported as grade 4, given that none of these 3 participants recorded any elevated temperature. Accordingly, only the 10 confirmed grade 4 fever events are discussed further: 8 (0.3%) in the mRNA-1273 group and 2 (0.2%) in the placebo group (Table S20).

Fever events (any temperature) in the mRNA-1273 group were reported more frequently after injection 2 than after injection 1. However, grade 4 fever events in the mRNA-1273 group occurred after both injections 1 and 2, with 3 of the 8 events occurring after injection 1 and 5 of the 8 events after injection 2.

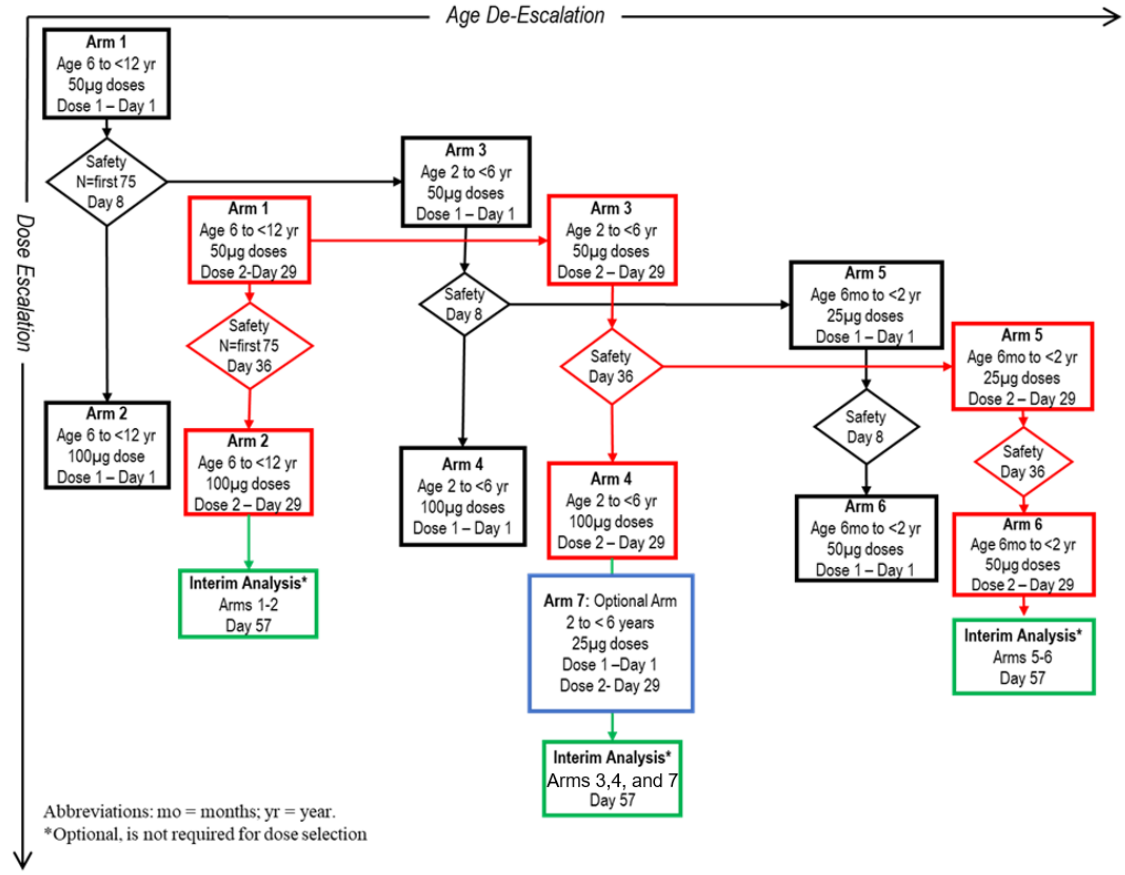
Four of the 10 participants reporting grade 4 fever also reported concurrent adverse events including: 3 (of 8) in the mRNA-1273 group (upper respiratory tract infection; croup; bilateral viral pneumonia) and 1 (of 2) in the placebo group (Covid-19 infection). These concurrent adverse events are confounders that may provide an alternative explanation for fever (Table S20). Among the grade 4 fever events, day of onset ranged from day 1 to day 5 post-vaccination with most starting on day 2 or 3 after injection. The duration of the febrile episodes ranged from 1 to 4 days with most episodes lasting for 2 days.

Unsolicited Pyrexia

In addition to analysis of fevers reported as solicited systemic ARs, we also examined unsolicited AEs of pyrexia. Unsolicited AEs of pyrexia occurred with similar frequency between groups: 36/1007 (3.6%) in placebo and 95/3031 (3.1%) in mRNA-1273 groups. Severe AEs of pyrexia occurred in 4/1007 (0.4%) of participants in placebo and 11/3031 (0.4%) in mRNA-1273 groups. Of these 15 severe AEs, most (13 of 15 events across both placebo and mRNA-1273 groups) occurred within 7 days of receiving study vaccine with resolution more than 7 days after study vaccine injection and are therefore accounted for in the discussion of solicited ARs of fever. Only 2 out of 15 events occurred more than 7 days post vaccination and therefore are only reported as unsolicited AEs occurring within 28 days of any dose. These events occurred on post-vaccination days 15 and 27, were both in mRNA-1273 group, and were both considered not related to study vaccine.

Figure S1. Study Design Schematic

(a) Part 1: Dose Escalation, Age De-escalation



(b) Part 2: Expansion

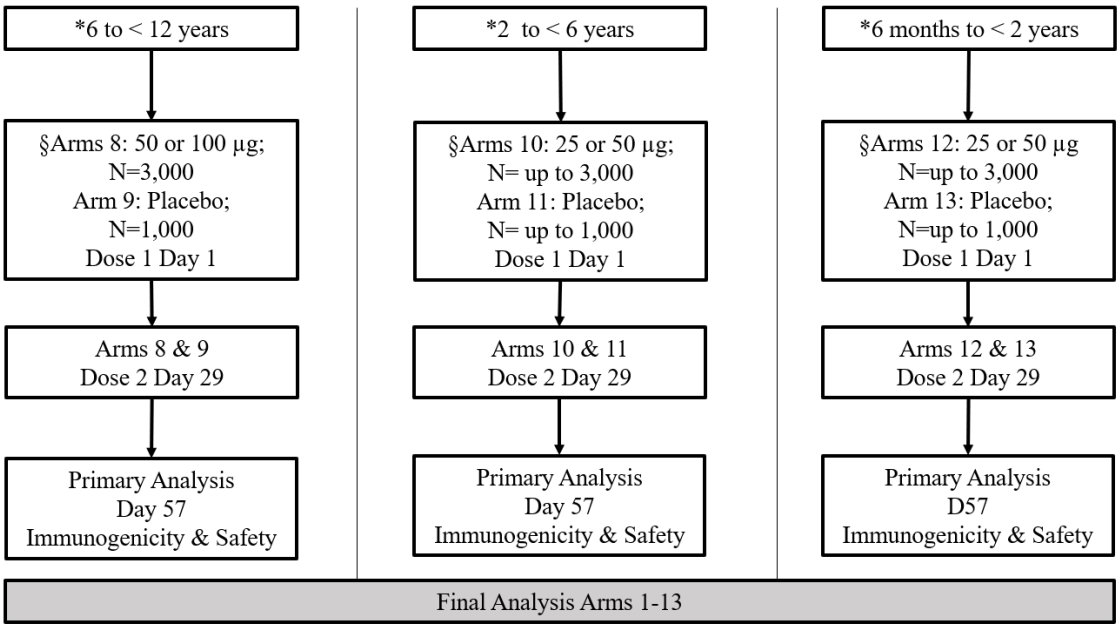
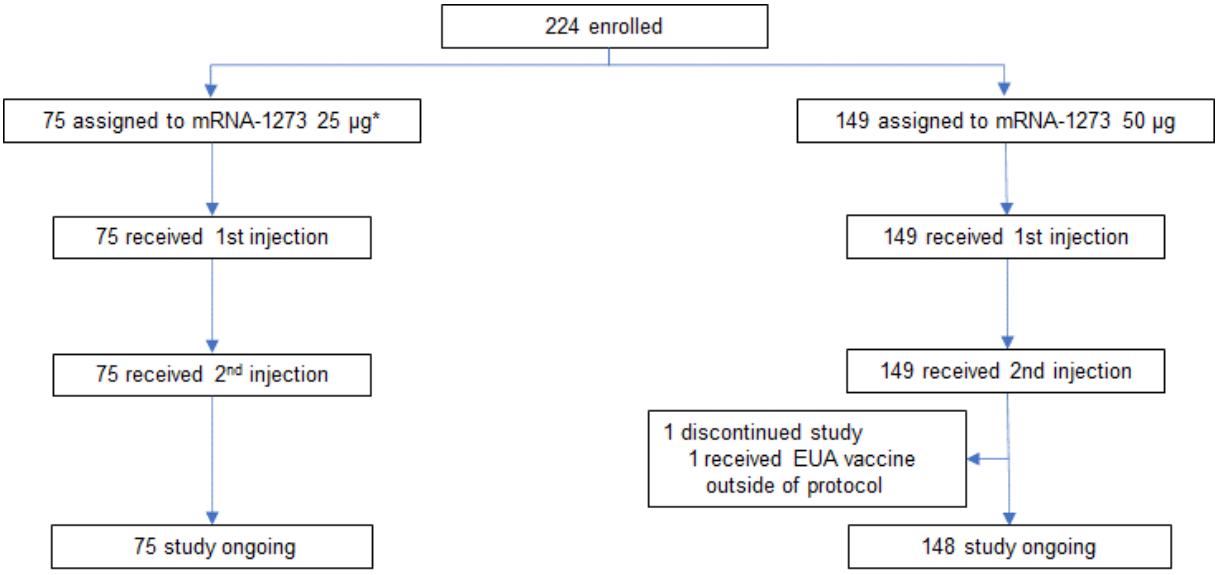


Figure S1. Study Design Schematic. CMI, cell-mediated immunity; D, day; Dose 1, injection 1 and Dose 2, injection 2; S, spike; VTEU, Vaccine and Treatment Evaluation Units. *Expansion and primary analysis for each age group may occur at different times. §Participants in each age group were assigned to one of 5 phlebotomy cohorts. Participants in 3 of these 5 cohorts provided blood specimens for immunogenicity on D1 (prior to randomization and first dose), D57, and one of D29 (prior to the second dose), D209, or D394 (such that each participant provides a total of 3 blood samples only). Participants in the Cohort D (remainder of the age group) provided a blood sample on D1 (prior to randomization and before the first dose) and within 4 days of receiving Dose 2 at D30 (+3 days) for storage and potential future biomarker testing. A fifth cohort of participants (selected VTEU sites only) provided blood samples for assessment of exploratory serology and CMI (S protein-specific T-cell responses) on D1 (prior to randomization and before the first dose), D43, D209, and D394.

Figure S2. Enrollment into the 2−5 Year and 6−23 Months Cohorts in Part 1

A. 2−5 years



B. 6 -23 months

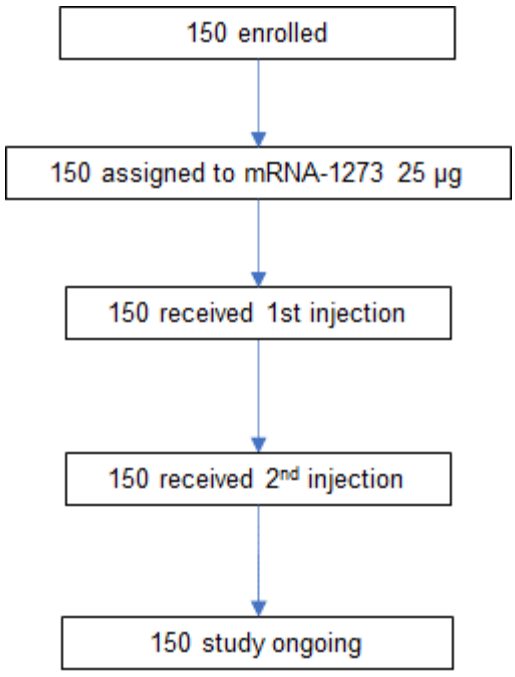


Figure S2. Enrollment into the 2−5 Year and 6−23 Months Cohorts in Part 1. Trial profile of participants in part 1 of KidCOVE who received mRNA-1273 25-µg or 50-µg in children 2−5 years (Panel A) and 25-µg in children 6−23 months (Panel B), based on the number of participants in the full analysis set for part 1. *6 participants enrolled in 25-µg group received at least one injection of 50-µg dose.

Figure S3. Solicited Local and Systemic Adverse Reactions by Baseline SARS-CoV-2-infection Status in Children 2−5 Years in Part 2 Solicited Safety Set

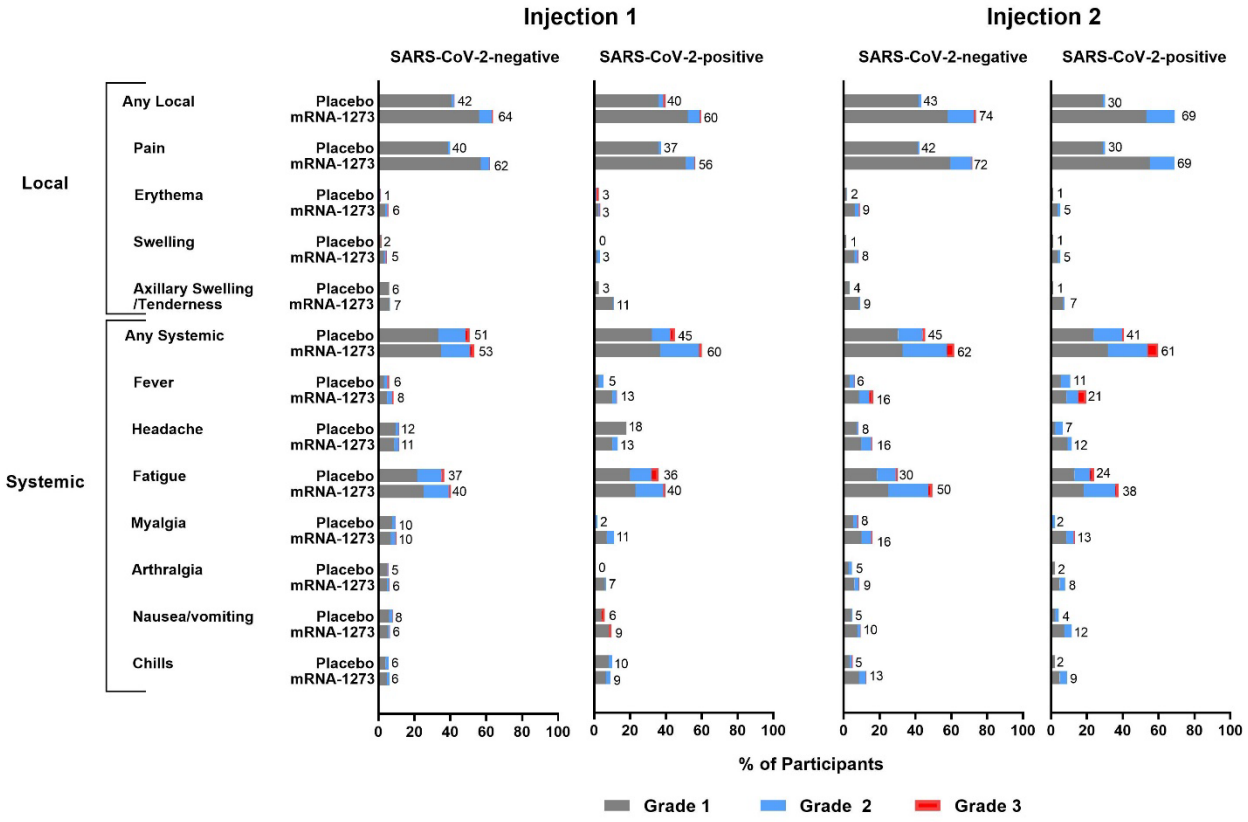


Figure S4. Solicited Local and Systemic Adverse Reactions by Baseline SARS-CoV-2-infection Status in Children 6–23 Months in Part 2 Solicited Safety Set

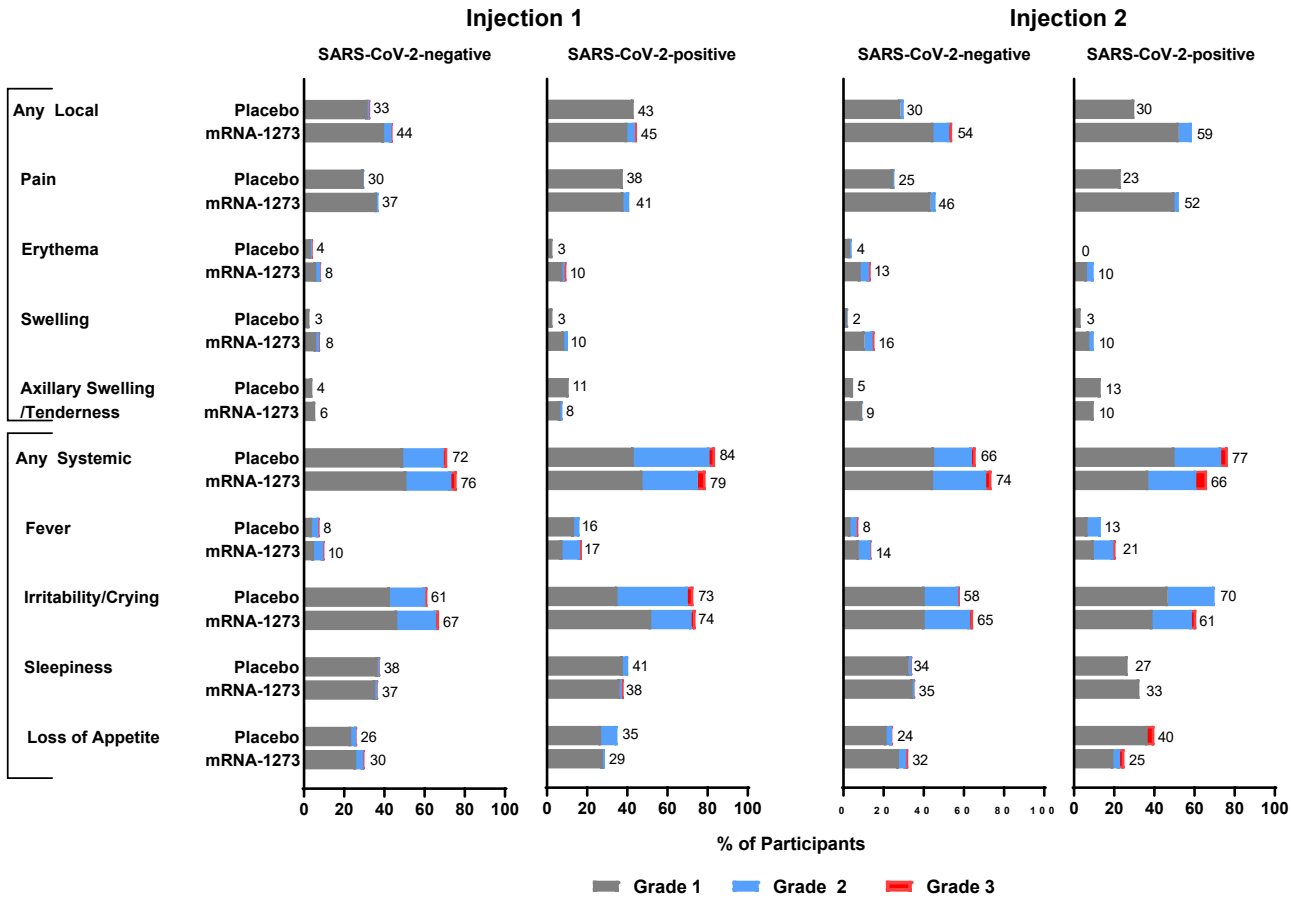


Figure S5. Maximum Fever Temperatures within 7 Days After Injections 1 and 2 in Children 2−5 Years and 6−23 Months in Part 2 Solicited Safety Set

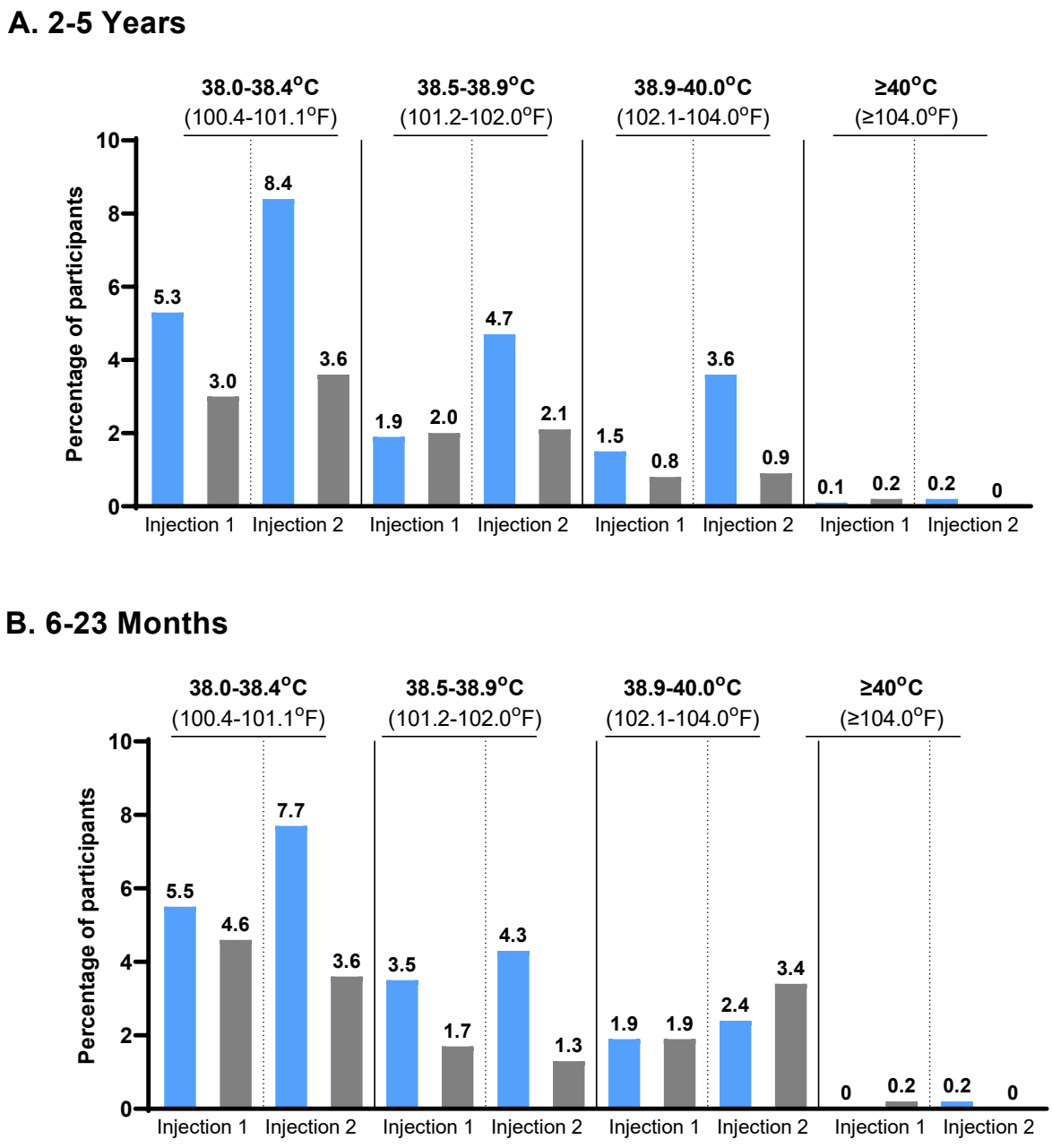


Figure S6. Percentage of Children Reporting Fevers by Temperature and Day After Injection 2 in Children 2−5 Years and 6−23 Months Part 2 Solicited Safety Set

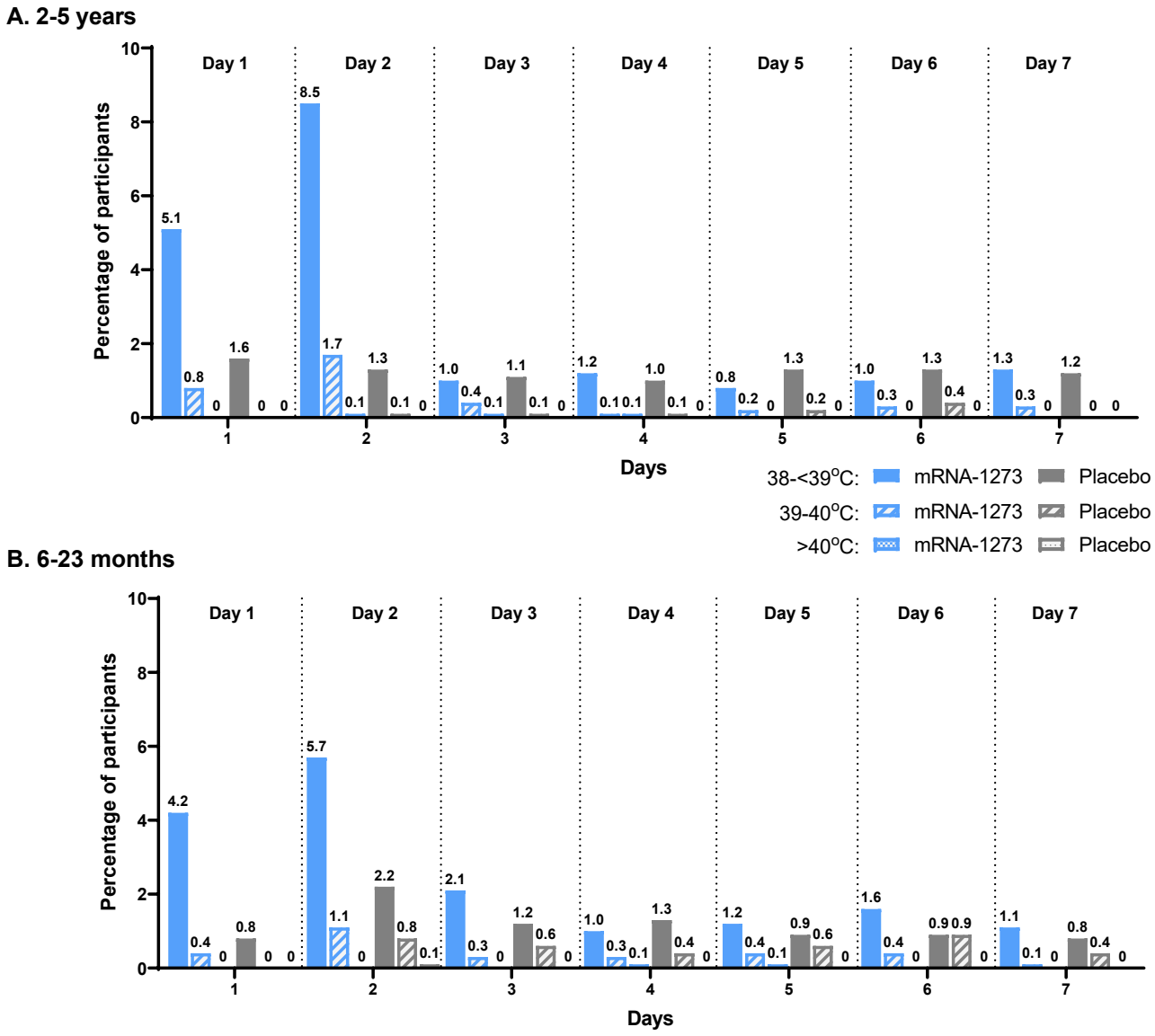
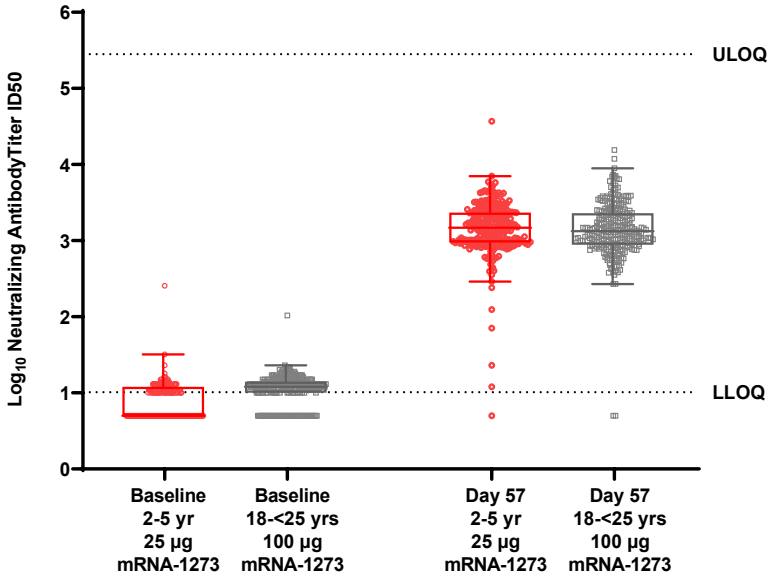


Figure S7. Distribution of Pseudovirus Neutralizing Antibody in Children 2−5 Years and 6−23 Months in Part 2 Per-Protocol Immunogenicity Set

A. 2−5 years



B. 6−23 months

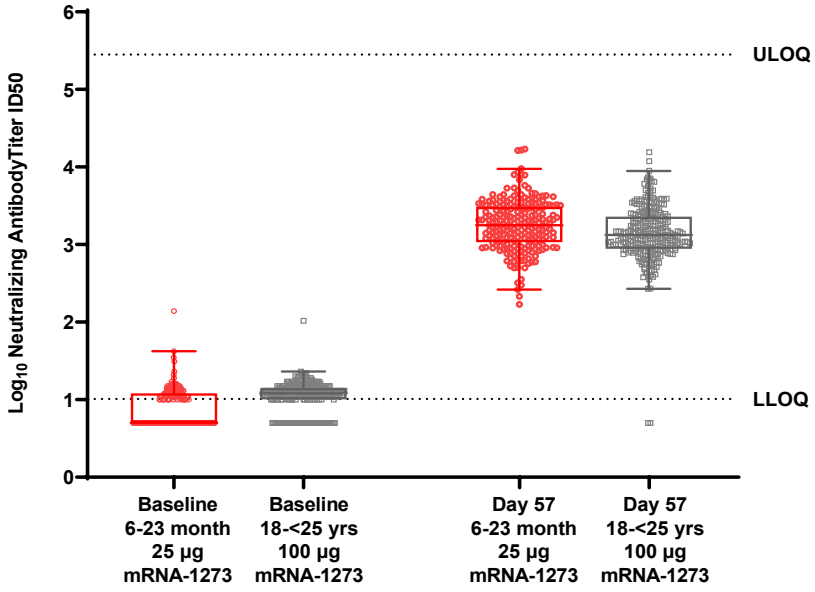


Figure S7. Pseudovirus Neutralizing Antibody in Children 2−5 Years and 6−23 Months, Part 2. Neutralizing antibody titers by PsVNA in 2−5-year-old (panel A) and 6−23-month-old (panel B) in all children regardless of prior SARS-CoV-2 infection status at baseline and day 57. Antibody values reported as below the lower limit of quantification (LLOQ) are replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification (ULOQ) are replaced by the ULOQ if actual values are not available. LLOQ = 10, ULOQ = 281600. Log10 (LLOQ) = 1.000, Log10 (ULOQ) = 5.450. COVE mRNA-1273 group includes young adults (18-25 years of age). Boxplot is based on log-transformed values. Boxes and horizontal bars denote interquartile (IQR) ranges and median endpoint titers; whisker endpoints are the maximum and minimum values below or above the median ±1.5 times the IQR.

Figure S8. Pseudovirus Neutralizing Antibody in Children 2−5 Years and 6−23 Months by Baseline SARS-CoV-2-infection Status in Part 2 Per-Protocol Immunogenicity Set

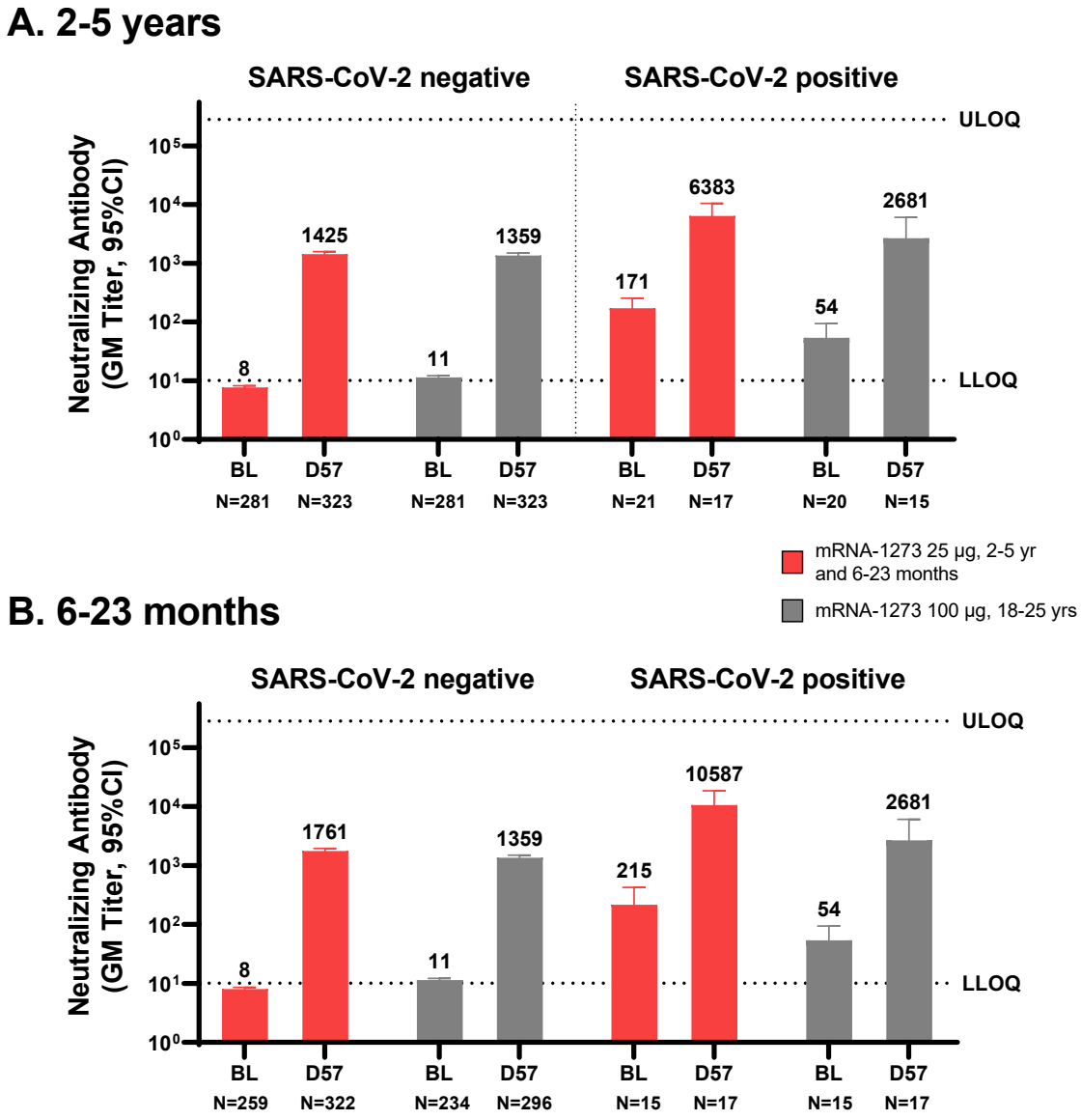
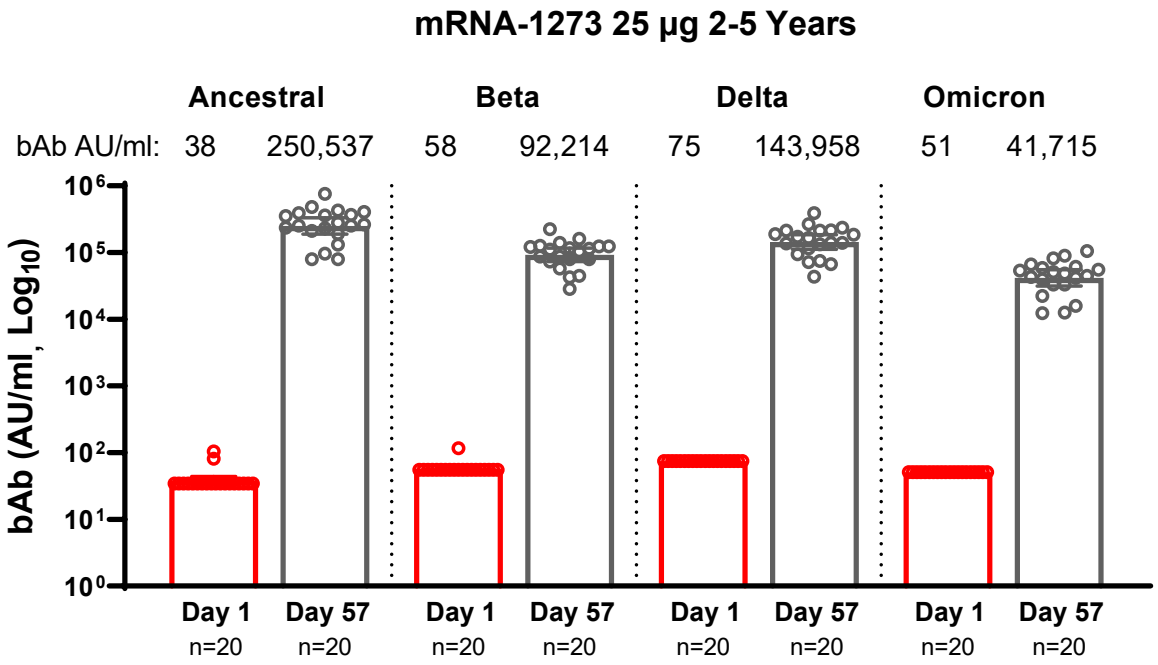


Figure S9. Binding Antibody Levels Against Ancestral SARS-CoV-2, Beta, Delta and Omicron Variants in Children 2−5 Years and 6−23 Months

A.



B.

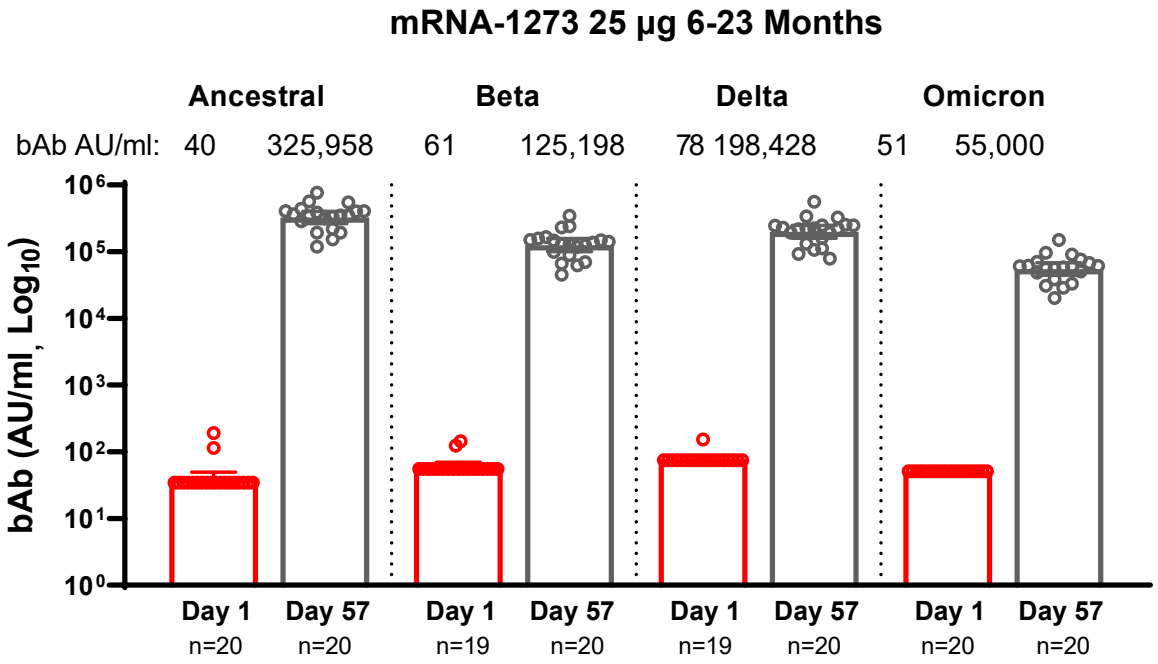
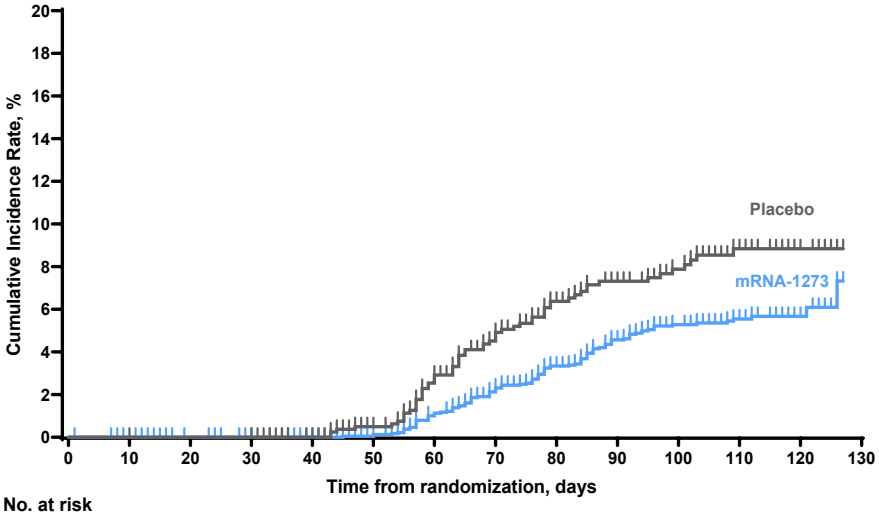


Figure S10. Cumulative Incidence of Covid-19 per the CDC Defintion Starting 14 Days After Second Injection in Per-Protocol Efficacy Set

A. Cumulative Incidence in Children 2−5 Years

PP Efficacy Set	Vaccine Efficacy (95% CI)	Incidence rate/1000 person-yr (95% CI)
mRNA-1273	36.8% (12.5%-54.0%)	175.0 (145.0-209.4)
Placebo		277.0 (211.0-355.8)



B. Cumulative Incidence in Children 6−23 Months

PP Efficacy Set	Vaccine Efficacy (95% CI)	Incidence rate/1000 person-yr (95% CI)
mRNA-1273	50.6% (21.4%-68.6%)	138.2 103.0-181.8)
Placebo		279.8 (193.8-391.0)

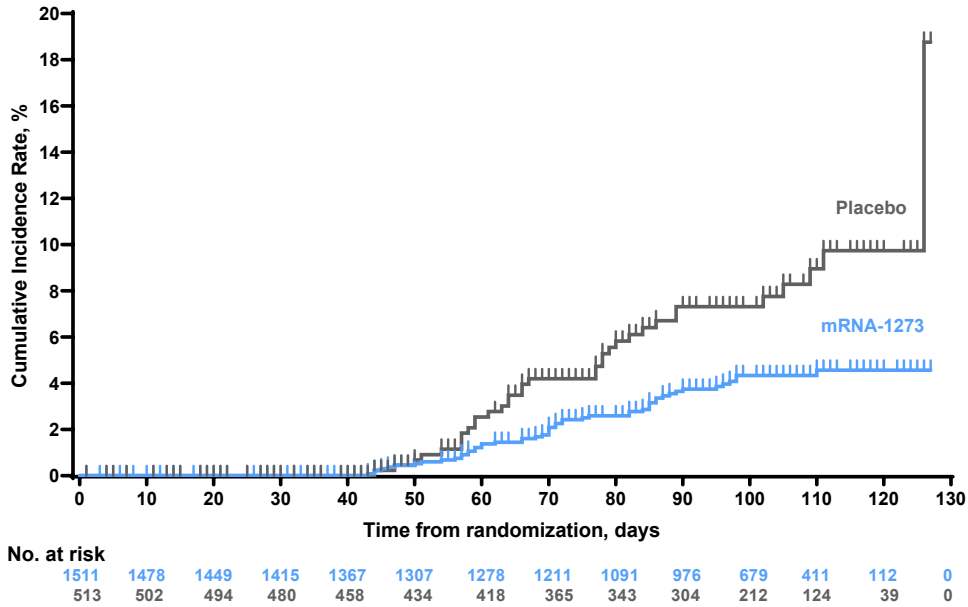


Table S1. Analysis Sets

Analysis Set	Description
Randomization Set	All participants who are randomized in Part 2, regardless of the participants' treatment status in the study
FAS	All enrolled participants who received at least 1 dose of IP (Part 1) All randomized participants who received at least 1 dose of IP (Part 2)
Per Protocol Set for Efficacy	All participants in the FAS who meet all the following criteria: • received planned doses of IP per schedule • complied with the second dose injection timing • had no major protocol deviations that impact key or critical efficacy data • had a negative RT-PCR test for SARS-CoV-2 and negative serology test based on bAb specific to SARS-CoV-2 nucleocapsid protein at baseline
Per Protocol Immunogenicity Subset	A subset of participants in the FAS who meet all the following criteria: • have baseline (Day 1) SARS-CoV-2 status available • have baseline and at least 1 post-injection Ab assessment for the analysis endpoint • received planned doses of IP per schedule • complied with the immunogenicity window based on the second dose injection timing • had a negative RT-PCR test for SARS-CoV-2 and negative serology test based on bAb specific to SARS-CoV-2 nucleocapsid protein at baseline • are not receiving HAART (for participants who have a diagnosis of HIV) • had baseline (Day 1) and Day 57 Ab assessment for the analysis endpoint • had no major protocol deviations that impact critical or key study data
mITT	All participants in the FAS who have no serologic or virologic evidence of prior SARS-CoV-2 infection (both negative RT-PCR test for SARS-CoV-2 and negative serology test based on bAb specific to SARS-CoV-2 nucleocapsid) at baseline
mITT1*	All participants in the mITT set excluding those who received the wrong treatment
Safety Set	All enrolled participants (Part 1) All randomized participants who received any study injection (Part 2)
Solicited Safety Set	All participants in the safety set who contributed any solicited AR data, ie, had at least 1 post-baseline solicited safety assessment
First Injection Solicited Safety Set	All participants in the Solicited Safety Set who have received the first study injection and have contributed any solicited AR data from the time of first study injection through the following 6 days
Second Injection Solicited Safety Set	All participants in the Solicited Safety Set who have received the second study injection and have contributed any solicited AR data from the time of second study injection through the following 6 days
*mITT1 set was used for the analysis of secondary endpoints in Figure 3B and Table S29 and is designated as "modified-intent-to-treat (miTT)".	

Table S2. Baseline Characteristics and Demographics of Children 2−5 Years in Part 1 Safety Set

Characteristic n (%)	mRNA-1273 25 µg N = 69	mRNA-1273 50 µg N = 155	Total N = 224
Age, years			
Mean (SD)	3.6 (1.04)	3.8 (1.10)	3.7 (1.08)
Median	4.0	4.0	4.0
IQR	3.0, 5.0	3.0, 5.0	3.0, 5.0
Age group, n (%)			
≥ 2 years and < 4 years	32 (46.4)	65 (41.9)	97 (43.3)
≥ 4 years and < 6 years	37 (53.6)	90 (58.1)	127 (56.7)
≥ 2 years and ≤ 36 months	9 (13.0)	26 (16.8)	35 (15.6)
> 36 months and < 6 years	60 (87.0)	129 (83.2)	189 (84.4)
Age (years), n (%)			
2	11 (15.9)	25 (16.1)	36 (16.1)
3	21 (30.4)	40 (25.8)	61 (27.2)
4	19 (27.5)	35 (22.6)	54 (24.1)
5	18 (26.1)	55 (35.5)	73 (32.6)
Sex, n (%)			
Male	36 (52.2)	80 (51.6)	116 (51.8)
Female	33 (47.8)	75 (48.4)	108 (48.2)
Race, n (%)			
White	49 (71.0)	133 (85.8)	182 (81.3)
Black	3 (4.3)	7 (4.5)	10 (4.5)
Asian	8 (11.6)	3 (1.9)	11 (4.9)
American Indian or Alaska Native	0	0	0
Native Hawaiian or other Pacific Islander	0	0	0
Multiracial	3 (4.3)	10 (6.5)	13 (5.8)
Other	6 (8.7)	2 (1.3)	8 (3.6)
Not reported	0	0	0
Unknown	0	0	0
Ethnicity, n (%)			
Hispanic or Latino	18 (26.1)	23 (14.8)	41 (18.3)
Not Hispanic or Latino	51 (73.9)	129 (83.2)	180 (80.4)
Not reported	0	3 (1.9)	3 (1.3)
Unknown	0	0	0
Race and ethnicity group*, n (%)			
White non-Hispanic	36 (52.2)	113 (72.9)	149 (66.5)
Communities of Color	33 (47.8)	42 (27.1)	75 (33.5)
Weight, kg			
Mean (SD)	18.0 (4.6)	18.2 (4.2)	18.1 (4.3)
Median	17.1	17.6	17.2
IQR	15.5-19.5	15.4-20.6	15.4-20.1
Baseline RT-PCR Results			
Negative	66 (95.7)	152 (98.1)	218 (97.3)
Positive	3 (4.3)	1 (0.6)	4 (1.8)
Missing	0	2 (1.3)	2 (0.9)
Baseline Elecsys Anti-SARS-CoV-2			
Negative	67 (97.1)	150 (96.8)	217 (96.9)
Positive	2 (2.9)	5 (3.2)	7 (3.1)
Baseline SARS-CoV-2 status†, n (%)			
Negative	64 (92.8)	147 (94.8)	211 (94.2)
Positive	5 (7.2)	6 (3.9)	11 (4.9)

Missing§	0	2 (1.3)	2 (0.9)

Covid-19 = coronavirus disease 2019; max = maximum; min = minimum; IQR=interquartile range; RT-PCR = reverse transcription-polymerase chain ratio; SARS-CoV-2 = severe acute respiratory syndrome coronavirus-2; SD = standard deviation. Percentages are based on the number of participants in the Part 1 Safety Set.
*White non-Hispanic is defined as White and non-Hispanic, and Communities of Color includes all the others whose race or ethnicity is not unknown, unreported, or missing.
†Baseline SARS-CoV-2 Status: Positive if there is immunologic or virologic evidence of prior Covid-19, defined as positive RT-PCR test or positive Elecsys result at Day 1. Negative is defined as negative RT-PCR test and negative Elecsys result at Day 1. §Missing: if one test is missing and the other is negative, then SARS-CoV-2 is missing; if one test is missing and the other test is positive, then SARS-CoV-2 is positive; if both are missing, then SARS-CoV-2 is missing. Data cutoff date: February 21, 2022.

Table S3. Baseline Characteristics and Demographics of Children 6−23 Months in Part 1 Safety Set

Characteristic n (%)	mRNA-1273 25 µg N = 150
Age months	
Mean (SD)	15.2 (4.88)
Median	14.5
IQR	11.0, 20.0
Age group, n (%)	
≥ 6 to 11 months	37 (24.7)
≥ 12 to 23 months	113 (75.3)
Sex, n (%)	
Male	83 (55.3)
Female	67 (44.7)
Race, n (%)	
White	125 (83.3)
Black	3 (2.0)
Asian	7 (4.7)
American Indian or Alaska Native	1 (0.7)
Native Hawaiian or other Pacific Islander	0
Multiracial	10 (6.7)
Other	3 (2.0)
Not reported	0
Unknown	1 (0.7)
Ethnicity, n (%)	
Hispanic or Latino	15 (10.0)
Not Hispanic or Latino	134 (89.3)
Not reported	0
Unknown	1 (0.7)
Race and ethnicity group[a], n (%)	
White non-Hispanic	112 (74.7)
Communities of Color	37 (24.7)
Missing	1 (0.7)
Weight, kg	
Mean (SD)	10.78 (1.996)
Median	10.76
Q1, Q3	9.55, 11.82
Min, max	6.6, 19.5
Baseline RT-PCR Results	
Negative	147 (98.0)
Positive	2 (1.3)
Missing	1 (0.7)
Baseline Elecsys Anti-SARS-CoV-2	
Negative	144 (96.0)
Positive	5 (3.3)
Missing	1 (0.7)
Baseline SARS-CoV-2 status[b], n (%)	
Negative	141 (94.0)
Positive	7 (4.7)
Missing	2 (1.3)

Covid-19 = coronavirus disease 2019; max = maximum; min = minimum; IQR=interquartile range; RT-PCR = reverse transcription-polymerase chain ratio; SARS-CoV-2 = severe acute respiratory syndrome coronavirus-2; SD = standard deviation. Percentages are based on the number of participants in the Part 1 Safety Set.
*White non-Hispanic is defined as White and non-Hispanic, and Communities of Color includes all the others whose race or ethnicity is not unknown, unreported, or missing.
†Baseline SARS-CoV-2 Status: Positive if there is immunologic or virologic evidence of prior Covid-19, defined as positive RT-PCR test or positive Elecsys result at Day 1. Negative is defined as negative RT-PCR test and negative Elecsys result at Day 1. Data cutoff date: February 21, 2022.

Table S4. Participant Demographics and Baseline Characteristics of Children 2−5 Years in Part 2 in Per-Protocol Immunogenicity Subset

Characteristic n (%)	mRNA-1273 25 µg (N = 264)
Age, years	
Mean (SD)	3.3 (0.95)
Median	3.0
Min, max	2, 5
Age group, n (%)	
≥ 2 years and < 4 years	158 (59.8)
≥ 4 years and < 6 years	106 (40.2)
≥ 2 years and ≤ 36 months	69 (26.1)
> 36 months and < 6 years	195 (73.9)
Age (years), n (%)	
<2*	0
2	64 (24.2)
3	94 (35.6)
4	77 (29.2)
5	29 (11.0)
Sex, n (%)	
Male	141 (53.4)
Female	123 (46.6)
Race, n (%)	
White	188 (71.2)
Black	20 (7.6)
Asian	16 (6.1)
American Indian or Alaska Native	1 (0.4)
Native Hawaiian or other Pacific Islander	0
Multiracial	34 (12.9)
Other	2 (0.8)
Not reported	2 (0.8)
Missing	1 (0.4)
Ethnicity, n (%)	
Hispanic or Latino	47 (17.8)
Not Hispanic or Latino	217 (82.2)
Race and ethnicity group†, n (%)	
White non-Hispanic	152 (57.6)
Communities of Color	112 (42.4)
Weight, kg	
Mean (SD)	16.50 (3.096)
Median	16.09
Min, max	10.7, 34.8
Baseline SARS-CoV-2 Status§, n (%)	
Negative	264 (100)
Positive	0

Max = maximum; Min = minimum; SD = standard deviation. Percentages are based on the number of participants in the Part 1 Per Protocol Immunogenicity Subset.

* Covid-19 = coronavirus disease 2019; max = maximum; min = minimum; RT-PCR = reverse transcription-polymerase chain ratio; SARS-CoV-2 = severe acute respiratory syndrome coronavirus-2; SD = standard deviation. Percentages are based on the number of participants in the Part 2 Safety Set.

† White non-Hispanic is defined as White and non-Hispanic, and Communities of Color includes all the others whose race or ethnicity is not unknown, unreported, or missing.

§Baseline SARS-CoV-2 Status: Positive if there is immunologic or virologic evidence of prior Covid-19, defined as positive RT-PCR test or positive Elecsys result at Day 1. Negative is defined as negative RT-PCR test and negative Elecsys result at Day 1. Data cutoff date: February 21st, 2022

Table S5. Solicited Local Adverse Reactions in Children 2−5 Years in Part 1 Solicited Safety Set

Local Adverse Reaction n, %	Injection 1		Injection 2	
	mRNA-1273 25 µg N=69	mRNA-1273 50 µg N=152	mRNA-1273 25 µg N=69	mRNA-1273 50 µg N=154
Solicited, N1	69	152	69	154
Solicited, any	44 (63.8)	117 (77.0)	58 (84.1)	144 (93.5)
Grade 1	36 (52.2)	82 (53.9)	37 (53.6)	65 (42.2)
Grade 2	8 (11.6)	31 (20.4)	20 (29.0)	64 (41.6)
Grade 3	0	4 (2.6)	1 (1.4)	14 (9.1)
Grade 4	0	0	0	1 (0.6)
Any Local, N1	69	152	69	154
Local, any	40 (58.0)	109 (71.7)	55 (79.7)	137 (89.0)
Grade 1	38 (55.1)	91 (59.9)	49 (71.0)	96 (62.3)
Grade 2	2 (2.9)	16 (10.5)	6 (8.7)	39 (25.3)
Grade 3	0	2 (1.3)	0	1 (1.3)
Grade 4	0	0	0	0
Pain, N1	69	152	69	154
Pain, any	39 (56.5)	104 (68.4)	54 (78.3)	136 (88.3)
Grade 1	37 (53.6)	91 (59.9)	48 (69.6)	103 (66.9)
Grade 2	2 (2.9)	12 (7.9)	6 (8.7)	32 (20.8)
Grade 3	0	1 (0.7)	0	1 (0.6)
Erythema, N1	69	152	69	154
Erythema, any	4 (5.8)	23 (15.1)	6 (8.7)	22 (14.3)
Grade 1	4 (5.8)	18 (11.8)	6 (8.7)	15 (9.7)
Grade 2	0	5 (3.3)	0	6 (3.9)
Grade 3	0	0	0	1 (0.6)
Swelling (Hardness), N1	69	152	69	154
Swelling (Hardness), any	4 (5.8)	17 (11.2)	6 (8.7)	18 (11.7)
Grade 1	4 (5.8)	14 (9.2)	6 (8.7)	11 (7.1)
Grade 2	0	2 (1.3)	0	7 (4.5)
Grade 3	0	1 (0.7)	0	0
Axillary Swelling*, N1	69	152	69	154
Axillary Swelling, any	1 (1.4)	10 (6.6)	1 (1.4)	16 (10.4)
Grade 1	1 (1.4)	10 (6.6)	0	13 (8.4)
Grade 2	0	0	1 (1.4)	3 (1.9)
Grade 3	0	0	0	0

*Axillary (or Groin) Swelling or Tenderness. N1 = Number of exposed participants who submitted any data for the event. Any = Grade 1 or higher. Percentages are based on N1.
Pain is injection site pain. Toxicity grade for injection site erythema (redness) or swelling (hardness) is defined as: grade 1=25-50 mm; grade 2=51-100 mm; grade 3=> 100 mm; grade 4=necrosis or exfoliative dermatitis. Toxicity grade for injection site pain and for axillary (underarm or groin) swelling or tenderness is defined as: grade 1=no interference with activity; grade 2=some interference with activity; grade 3=prevents daily activity; grade 4=emergency room visit or hospitalization. Data cutoff date: February 21st, 2022

Table S6. Solicited Systemic Adverse Reactions in Children 37 months-5 Years in Part 1 Solicited Safety Set

Systemic Adverse Reactions n (%)	Injection 1		Injection 2	
	mRNA-1273 25 µg N=60	mRNA-1273 50 µg N=128	mRNA-1273 25 µg N=60	mRNA-1273 50 µg N=128
Any Systemic AR, N1	60	128	60	128
Systemic AR, any	16 (26.7)	54 (42.2)	29 (48.3)	85 (66.4)
Grade 1	11 (18.3)	35 (27.3)	14 (23.3)	31 (24.2)
Grade 2	5 (8.3)	17 (13.3)	14 (23.3)	43 (33.6)
Grade 3	0	2 (1.6)	1 (1.7)	11 (8.6)
Grade 4	0	0	0	0
Fever, N1	60	126	60	128
Fever, any	1 (1.7)	8 (6.3)	6 (10.0)	32 (25.0)
Grade 1	1 (1.7)	6 (4.7)	2 (3.3)	9 (7.0)
Grade 2	0	2 (1.6)	3 (5.0)	15 (11.7)
Grade 3	0	0	1 (1.7)	8 (6.3)†
Grade 4	0	0	0	0
Headache, N1	60	126	60	127
Headache	5 (8.3)	13 (10.3)	11 (18.3)	33 (26.0)
Grade 1	5 (8.3)	10 (7.9)	9 (15.0)	22 (17.3)
Grade 2	0	3 (2.4)	2 (3.3)	10 (7.9)
Grade 3	0	0	0	1 (0.8)
Fatigue, N1	60	126	60	127
Fatigue	8 (13.3)	43 (34.1)	21 (35.0)	70 (55.1)
Grade 1	5 (8.3)	27 (21.4)	11 (18.3)	31 (24.4)
Grade 2	3 (5.0)	14 (11.1)	10 (16.7)	34 (26.8)
Grade 3	0	2 (1.6)	0	5 (3.9)
Myalgia, N1	60	126	60	127
Myalgia	4 (6.7)	12 (9.5)	9 (15.0)	24 (18.9)
Grade 1	4 (6.7)	11 (8.7)	5 (8.3)	11 (8.7)
Grade 2	0	0	4 (6.7)	12 (9.4)
Grade 3	0	1 (0.8)	0	1 (0.8)
Arthralgia, N1	60	126	60	127
Arthralgia	2 (3.3)	5 (4.0)	3 (5.0)	11 (8.7)
Grade 1	0	4 (3.2)	2 (3.3)	10 (7.9)
Grade 2	2 (3.3)	0	1 (1.7)	1 (0.8)
Grade 3	0	1 (0.8)	0	0
Nausea/vomiting, N1	60	126	60	127
Nausea /vomiting	2 (3.3)	7 (5.6)	5 (8.3)	16 (12.6)
Grade 1	2 (3.3)	6 (4.8)	4 (6.7)	14 (11.0)
Grade 2	0	1 (0.8)	1 (1.7)	2 (1.6)
Grade 3	0	0	0	0
Chills, N1	60	126	60	127
Chills	0	4 (3.2)	3 (5.0)	20 (15.7)
Grade 1	0	2 (1.6)	2 (3.3)	11 (8.7)
Grade 2	0	2 (1.6)	1 (1.7)	9 (7.1)
Grade 3	0	0	0	0

*= Axillary (or Groin) Swelling or Tenderness. N1 = Number of exposed participants who submitted any data for the event. Any = Grade 1 or higher. Percentages are based on N1. Toxicity grade for solicited systemic adverse reactions other than fever is defined as: grade 1 = no interference with activity (or, for nausea/vomiting: 1 2 episodes/24 hours); grade 2 = some interference with activity (or, for nausea/vomiting: > 2 episodes/24 hours); grade 3 = prevents daily activity; grade 4 = emergency room visit or hospitalization. Protocol-defined toxicity grades for fever in participants 37 months to <6 years of age were: grade 1 = 38°C to 38.4°C, grade 2 = 38.5°C to 38.9°C, grade 3 = 39°C to 40°C, and grade 4 > 40°C.Data cutoff date: February 21, 2022.

Table S7. Solicited Systemic Adverse Reactions in Children 24-36 Months in Part 1 Solicited Safety Set

Systemic Adverse Reactions n (%)	Injection 1		Injection 2	
	mRNA-1273 25 µg N=9	mRNA-1273 50 µg N=24	mRNA-1273 25 µg N=9	mRNA-1273 50 µg N=26
Any Systemic, N1	9	24	9	26
Systemic, any	5 (55.6)	8 (33.3)	8 (88.9)	20 (76.9)
Grade 1	4 (44.4)	6 (25.9)	5 (55.6)	15 (57.7)
Grade 2	1 (11.1)	1 (4.2)	3 (33.3)	2 (7.7)
Grade 3	0	1 (4.2)	0	2 (7.7)
Grade 4	0	0	0	1 (3.8)
Fever, N1	9	24	9	26
Fever	1 (11.1)	2 (8.3)	0	9 (34.6)
Grade 1	1 (11.1)	1 (4.2)	0	4 (11.4)
Grade 2	0	0	0	2 (5.7)
Grade 3	0	1 (4.2)	0	2 (5.7)
Grade 4	0	0	0	1 (2.9)
Irritability/Crying,N1	9	23	9	26
Irritability/Crying	5 (55.6)	6 (26.1)	6 (66.7)	18 (69.2)
Grade 1	4 (44.4)	5 (21.7)	3 (33.3)	15 (57.7)
Grade 2	1 (11.1)	1 (4.3)	3 (33.3)	3 (11.5)
Grade 3	0	0	0	0
Sleepiness, N1	9	23	9	26
Sleepiness	2 (22.2)	3 (13.0)	2 (22.2)	10 (38.5)
Grade 1	2 (22.2)	3 (13.0)	2 (22.2)	8 (30.8)
Grade 2	0	0	0	2 (7.7)
Grade 3	0	0	0	0
Loss of Appetite, N1	9	23	9	26
Loss of Appetite	1 (11.1)	0	2 (22.2)	7 (26.9)
Grade 1	1 (11.1)	0	1 (11.1)	4 (15.4)
Grade 2	0	0	1 (11.1)	1 (3.8)
Grade 3	0	0	0	2 (7.7)

*= Axillary (or Groin) Swelling or Tenderness. N1 = Number of exposed participants who submitted any data for the event. Any = Grade 1 or higher. Percentages are based on N1.

Toxicity grade for solicited systemic adverse reactions other than fever is defined as: grade 1 = no interference with activity (or, for nausea/vomiting: 12 episodes/24 hours); grade 2 = some interference with activity (or, for nausea/vomiting: > 2 episodes/24 hours); grade 3 = prevents daily activity; grade 4 = emergency room visit or hospitalization. Protocol-defined toxicity grades for fever in participants 2 years to ≤36 months were: grade 1 = 38°C to 38.5°C, grade 2 = 38.6°C to 39.5°C, grade 3 = 39.6°C to 40°C, and grade 4 >40.0°C. Data cutoff date: February 21, 2022.

Table S8. Solicited Local and Systemic Adverse Reactions in Children 6−23 Months in Part 1 Solicited Safety Set

Solicited ARs N (%)	Injection 1	Injection 2
	mRNA-1273 25 µg N=149	mRNA-1273 25 µg N=150
Solicited, N1	149	150
Solicited, any	123 (82.6)	122 (81.3)
Grade 1	91 (61.1)	64 (42.7)
Grade 2	31 (20.8)	52 (34.7)
Grade 3	1 (0.7)	6 (4.0)
Grade 4	0	0
Any Local, N1	149	150
Local, any	60 (40.3)	71 (47.3)
Grade 1	56 (37.6)	54 (36.0)
Grade 2	4 (2.7)	14 (9.3)
Grade 3	0	3 (2.0)
Grade 4	0	0
Pain, N1	149	150
Pain, any	48 (32.2)	58 (38.7)
Grade 1	45 (30.2)	52 (34.7)
Grade 2	3 (2.0)	6 (4.0)
Grade 3	0	0
Erythema, N1	149	150
Erythema, any	11 (7.4)	20 (13.3)
Grade 1	11 (7.4)	11 (7.3)
Grade 2	0	8 (5.3)
Grade 3	0	1 (0.7)
Swelling (Hardness), N1	149	150
Swelling (Hardness), any	14 (9.4)	18 (12.0)
Grade 1	12 (8.1)	10 (6.7)
Grade 2	2 (1.3)	6 (4.0)
Grade 3	0	2 (1.3)
Axillary Swelling*, N1	149	150
Axillary Swelling*, any	15 (10.1)	11 (7.3)
Grade 1	15 (10.1)	10 (6.7)
Grade 2	0	1 (0.7)
Grade 3	0	0
Any systemic, N1	149	150
Systemic, any	107 (71.8)	104 (69.3)
Grade 1	77 (51.7)	58 (38.7)
Grade 2	29 (19.5)	43 (28.7)
Grade 3	1 (0.7)	3 (2.0)
Grade 4	0	0
Fever, N1	149	150
Fever, any	11 (7.4)	17 (11.3)
Grade 1	8 (5.4)	7 (4.7)
Grade 2	3 (2.0)	9 (6.0)
Grade 3	0	1 (0.7)
Grade 4	0	0
Irritability/Crying, N1	149	150
Irritability/Crying, any	94 (63.1)	94 (62.7)
Grade 1	66 (44.3)	56 (37.3)

Grade 2	28 (18.8)	38 (25.3)
Grade 3	0	0
Sleepiness, N1	149	150
Sleepiness, any	39 (26.2)	42 (28.0)
Grade 1	38 (25.5)	39 (26.0)
Grade 2	0	3 (2.0)
Grade 3	1 (0.7)	0
Loss of Appetite, N1	149	150
Loss of Appetite, any	28 (18.8)	38 (25.3)
Grade 1	26 (17.4)	31 (20.7)
Grade 2	2 (1.3)	5 (3.3)
Grade 3	0	2 (1.3)

*Axillary (or Groin) Swelling or Tenderness. N1 = Number of exposed participants who submitted any data for the event. Any = Grade 1 or higher. Percentages are based on N1.
Pain is injection site pain. Toxicity grade for injection site erythema (redness) or swelling (hardness) is defined as: grade 1=25-50 mm; grade 2=51-100 mm; grade 3=> 100 mm; grade 4=necrosis or exfoliative dermatitis. Toxicity grade for injection site pain and for axillary (underarm or groin) swelling or tenderness is defined as: grade 1=no interference with activity; grade 2=some interference with activity; grade 3=prevents daily activity; grade 4=emergency room visit or hospitalization. Data cutoff date: February 21, 2022

Table S9. Summary Duration (Days) of Local and Systemic Adverse Reactions in Children 2−5 Years Following Injections 1 and 2 in Part 1 Solicited Safety Set

Duration days	Injection 1			Injection 2		
	mRNA-1273 25 µg N=69	mRNA-1273 50 µg N=152	Total N=221	mRNA-1273 25 µg N=69	mRNA-1273 50 µg N=154	Total N=223
Any solicited, n	44	117	161	58	144	202
Mean days (SD)	2.7 (1.9)	3.5 (5.1)	3.3 (4.5)	2.8 (1.9)	3.3 (2.7)	3.1 (2.5)
Median days (IQR)	2.0 (1.0-4.0)	2.0 (1.0-4.0)	2.0 (1.0-4.0)	2.0 (1.0-4.0)	2.0 (2.0-4.0)	2.0 (2.0-4.0)
Any local AR, n	40	109	149	55	137	192
Mean days (SD)	1.9 (1.4)	2.6 (3.0)	2.4 (2.7)	2.1 (1.4)	2.8 (2.6)	2.6 (2.4)
Median days (IQR)	1.0 (1.0-2.0)	2.0 (1.0-3.0)	2.0 (1.0-3.0)	2.0 (1.0-2.0)	2.0 (2.0-3.0)	2.0 (1.0-3.0)
Pain, n	39	104	143	54	136	190
Mean days (SD)	1.8 (1.3)	2.1 (1.1)	2.0 (1.2)	1.9 (1.2)	2.3 (1.2)	2.2 (1.2)
Median days (IQR)	1.0 (1.0-2.0)	2.0 (1.0-3.0)	2.0 (1.0-3.0)	2.0 (1.0-2.0)	2.0 (1.0-3.0)	2.0 (1.0-3.0)
Erythema (redness), n	4	23	27	6	22	28
Mean days (SD)	1.5 (0.6)	2.7 (2.7)	2.6 (2.6)	2.5 (1.1)	1.9 (0.9)	2.0 (1.0)
Median days (IQR)	1.5 (1.0-2.0)	2.0 (1.0-3.0)	2.0 (1.0-3.0)	2.5 (2.0-3.0)	2.0 (1.0-3.0)	2.0 (1.0-3.0)
Swelling (hardness), n	4	17	21	6	18	24
Mean days (SD)	2.0 (1.4)	2.0 (2.2)	2.0 (2.0)	1.5 (0.6)	1.7 (0.9)	1.7 (0.8)
Median days (IQR)	1.5 (1.0-3.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.5 (1.0-2.0)	1.5 (1.0-2.0)	1.5 (1.0-2.0)
Axillary (or groin) swelling/tenderness (n)	1	10	11	1	16	17
Mean days (SD)	1.0 (NA)	3.8 (8.5)	3.5 (8.1)	2.0 (NA)	4.1 (6.5)	3.9 (6.3)
Median days (IQR)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	2.0 (2.0-2.0)	1.5 (1.0-4.5)	2.0 (1.0-4.0)
Any systemic AR, n	21	62	83	37	105	142
Mean days (SD)	2.1 (1.7)	3.1 (6.0)	2.8 (5.3)	2.0 (1.6)	2.3 (1.8)	2.2 (1.7)
Median days (IQR)	1.0 (1.0-3.0)	1.0 (1.0-3.0)	1.0 (1.0-3.0)	1.0 (1.0-2.0)	2.0 (1.0-3.0)	2.0 (1.0-3.0)
Fever, n	2	10	12	6	41	47
Mean days (SD)	1.0 (0)	7.6 (13.9)	6.5 (12.9)	1.2 (0.4)	1.4 (0.8)	1.3 (0.8)
Median days (IQR)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)
Headache, n	5	13	18	11	33	44
Mean days (SD)	2.6 (2.6)	1.2 (0.4)	1.6 (1.5)	1.8 (1.7)	1.7 (1.3)	1.7 (1.4)
Median days (IQR)	1.0 (1.0-3.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)
Fatigue, n	8	43	51	21	70	91
Mean days (SD)	1.5 (0.5)	1.8 (1.5)	1.7 (1.4)	1.2 (0.4)	2.3 (1.8)	2.0 (1.2)
Median days (IQR)	1.5 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-1.0)	2.0 (1.0-3.0)	1.0 (1.0-2.0)
Myalgia, n	4	12	16	9	24	33
Mean days (SD)	1.0 (0)	1.2 (0.4)	1.1 (0.3)	1.9 (2.0)	1.5 (1.4)	1.6 (1.6)
Median days (IQR)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-2.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)
Arthralgia, n	2	5	7	3	11	14
Median days	1.0 (0)	1.0 (0)	1.0 (0)	1.7 (1.2)	1.5 (1.5)	1.5 (1.4)
Median days (IQR)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-3.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)
Nausea/vomiting, n	2	7	9	5	16	21
Mean days (SD)	2.5 (2.1)	1.3 (0.8)	1.6 (1.1)	1.0 (0)	1.3 (1.3)	1.2 (1.1)
Median days (IQR)	2.5 (1.0-4.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)
Chills, n	0	4	4	3	20	23
Mean days (SD)	0	2.2 (1.2)	2.1 (1.6)	1.0 (0)	1.3 (0.9)	1.3 (0.9)
Median days (IQR)	0 (0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-1.0	1.0 (1.0-1.0	1.0 (1.0-1.0
Irritability/Crying	5	6	11	6	18	24
Mean days (SD)	2.0 (2.2)	2.2 (1.2)	2.1 (1.6)	2.3 (2.0)	2.1 (1.2)	2.1 (1.4)
Median days (IQR)	1.0 (1.0-1.0)	2.0 (1.0-3.0)	1.0 (1.0-3.0)	1.5 (1.0-3.0)	2.0 (1.0-3.0)	2.0 (1.0-3.0
Sleepiness	2	3	5	2	10	12
Mean days (SD)	1.0 (0)	2.0 (1.0)	1.6 (0.9)	1.5 (0.7)	2.2 (1.6)	2.1 (1.5)
Median days (IQR)	1.0 (1.0-1.0)	2.0 (1.0-3.0)	1.0 (1.0-2.0)	1.5 (1.0-2.0)	1.5 (1.0-3.0)	1.5 (1.0-2.5)
Loss of Appetite	1	0	1	2	7	9
Mean days (SD)	1.0 (NA)	0	1.0 (NA)	2.5 (2.1)	3.1 (2.2)	3.0 (2.1)
Median days (IQR)	1.0 (1.0-1.0)	0 (0)	1.0 (1.0-1.0)	2.5 (1.0-4.0)	2.0 (1.0-6.0)	2.0 (1.0-4.0)

AR, adverse reaction; IQR-interquartile range; N, number of exposed participants who reported the event on any day within 7 days of the first injection. n = Number of exposed participants who reported the event on any day within 7 days of the first injection. NA=not applicable. Duration is calculated as the last day — the first day + 1 when the solicited adverse reaction was reported starting within the 7 days of injection. If the solicited adverse reaction continued beyond 7 days, the days after 7 days were included. Pain for children ages 6 to ≤36 months is injection-site pain or tenderness, and for 37 months to <12 years is injection-site pain. The number of days which is higher for solicited events after either the first or the second injection is summarized. Data cut-off date: February 21, 2022.

Table S10. Summary Duration (Days) of Local and Systemic Adverse Reactions in Children 6−23 Months Following Injections 1 and 2 in Part 1 Solicited Safety Set

Duration days	Injection 1	Injection 2
	mRNA-1273 25 µg N=149	mRNA-1273 25 µg N=150
Any solicited, n	123	122
Mean days (SD)	3.5 (3.1)	4.2 (3.0)
Median days (IQR)	2.0 (1.0-5.0)	4.0 (2.0-6.0)
Any local, n	60	71
Mean days (SD)	2.4 (2.7)	2.7 (2.5)
Median days (IQR)	1.0 (1.0-3.0)	2.0 (1.0-3.0)
Pain, n	48	58
Mean days (SD)	1.7 (1.4)	2.2 (1.7)
Median days (IQR)	1.0 (1.0-2.0)	1.5 (1.0-3.0)
Erythema (redness), n	11	20
Mean days (SD)	1.4 (0.8)	2.5 (2.1)
Median days (IQR)	1.0 (1.0-1.0)	2.0 (1.0-3.0)
Swelling (hardness), n	14	18
Mean days (SD)	2.3 (1.8)	2.2 (1.5)
Median days (IQR)	2.0 (1.0-3.0)	2.0 (1.0-2.0)
Axillary (or groin) swelling/tenderness, n	15	11
Mean days (SD)	3.1 (4.7)	4.8 (3.9)
Median days (IQR)	1.0 (1.0-3.0)	4.0 (1.0-7.0)
Any systemic, n	107	104
Mean days (SD)	3.2 (2.7)	3.9 (3.0)
Median days (IQR)	2.0 (1.0-5.0)	3.0 (1.0-5.0)
Fever, n	11	17
Mean days (SD)	1.5 (1.0)	1.4 (0.7)
Median days (IQR)	1.0 (1.0-2.0)	1.0 (1.0-2.0)
Irritability/Crying	94	94
Mean days (SD)	3.1 (2.6)	3.5 (2.8)
Median days (IQR)	2.0 (1.0-5.0)	3.0 (1.0-5.0)
Sleepiness	39	42
Mean days (SD)	1.9 (1.5)	2.4 (2.2)
Median days (IQR)	1.0 (1.0-3.0)	1.0 (1.0-4.0)
Loss of Appetite	28	38
Mean days (SD)	2.5 (2.4)	2.8 (2.7)
Median days (IQR)	1.0 (1.0-4.0)	2.0 (1.0-4.0)

AR, adverse reaction; IQR, interquartile range; N, number of exposed participants who reported the event on any day within 7 days of the first injection. Duration is calculated as the last day — the first day + 1 when the solicited adverse reaction was reported starting within the 7 days of injection. If the solicited adverse reaction continues beyond 7 days, the days after 7 days are included. The number of days which is higher with solicited events after either the first or the second injection is summarized. Data cut-off date: February 21, 2022.

Table S11. Summary of Unsolicited Adverse Events <28 Days After Any Injection in Children 2−5 Years and 6−23 Months in Part 1 Safety Set

	2-5 years		6-23 months
Unsolicited Adverse events n (%)	**mRNA-1273 50 µg**	**mRNA-1273 25 µg**	**mRNA-1273 25 µg**
	N=69	**N=155**	**N=150**
Unsolicited AEs regardless of relationship to study vaccination			
All	16 (23.2)	56 (36.1)	80 (53.3)
Serious	0	0	2 (1.3)
Fatal	0	0	0
Medically attended	5 (7.2)	32 (20.6)	45 (30.0)
Leading to discontinuation from study vaccine	0	0	0
Leading to discontinuation from study	0	0	0
Severe	0	4 (2.6)	4 (2.7)
Non-serious	16 (23.2)	56 (36.1)	80 (53.3)
Severe	0	4 (2.6)	2 (1.3)
Special interest (AESI)	0	0	1 (0.7)
MIS-C	0	0	0
Other	0	0	1 (0.7)*
Unsolicited AEs related to study vaccination			
All	5 (7.2)	17 (11.0)	23 (15.3)
Serious	0	0	0
Fatal	0	0	0
Medically attended	0	3 (1.9)	4 (2.7)
Leading to discontinuation from study vaccine	0	0	0
Leading to discontinuation from study	0	0	0
Severe	0	3 (1.9)	2 (1.3)
Non-serious	5 (7.2)	17 (11.0)	23 (15.3)
Severe	0	3 (1.9)	2 (1.3)
Special interest (AESI)	0	0	0
MIS-C	0	0	0
Other	0	0	0

AE, adverse event; AESI, adverse event of special interest; MIS-C, multisystem inflammatory syndrome in children. AE is defined as any event not present before exposure to study vaccination or any event already present that worsened in intensity or frequency after exposure. Percentages are based on the number of participants in the safety set. Solicited adverse reactions with toxicity grade = 0 that lasted beyond day 7 or started after day 7 are not included in this table. *1-year-old male in mRNA-1273 group experienced grade 3 AESI (also an SAE for overnight hospitalization) of febrile convulsion 10 days after injection 2 that resolved the same day considered by investigator to not be related to study vaccination with occurrence of maculo-papular rash onset 2 days before the event of febrile seizure (8 days post-infection 2). After the analysis cutoff date, a 3-year-old participant was diagnosed with MIS-C that started 113 days after placebo injection 2, considered not related by the investigator. The participant had a grade 1 asymptomatic SARS-CoV-2 infection 37 days prior to the onset of symptoms. Five days after onset of MIS-C symptoms, the child was hospitalized then discharged after 4 days with a diagnosis of MIS-C and was recovering. Data cut-off date: February 21, 2022.

Table S12. Analysis of Neutralizing Antibody Titers and Seroresponse Rate at Day 57 by Pseudovirus Neutralization Assay (ID_{50}) in Children 2−5 Years in Part 1 Per-protocol Immunogenicity Subset

	2 to < 6 Years mRNA-1273 25 µg N = 50	2 to < 6 Years mRNA-1273 50 µg N = 69	18 to ≤ 25 Years mRNA-1273 100 µg N = 295
Baseline GMT	9.3 (NE-NE)	9.3 (NE-NE)	9.3 (9.2-9.4)
GMT (95% CI) at Day 57*	1013.8 (846.2-1214.5)	1844.2 (1602.3- 2122.4)	1299.9 (1170.6- 1443.4)
GMFR (95% CI)* at Day 57 from baseline	109.6 (91.5-131.3)	199.4 (173.3-229.5)	140.0 (126.1-155.4)
GMR (children vs 18-25 years; model-based) (95% CI)†	0.8 (0.6-1.0)	1.4 (1.1-1.8)	NA
Participants achieving seroresponse, n (%)§ at Day 57	50/50 (100)	69/69 (100)	292/295 (99.0)
95% CI¶	(92.9-100.0)	(94.8-100.0)	(97.1- 99.8)
Difference in seroresponse rate (children vs 18-25 years), % (95% CI)‖	1.0 (-6.1-3.0)	1.0 (-4.3-3.0)	NA

ANCOVA = analysis of covariance; CI = confidence interval; GMFR = geometric mean fold rise; GMR = geometric mean ratio; GMT = geometric mean titer (noted as observed or model based [estimated by geometric least squares mean and used to estimate GMR); ID50 = 50% inhibitory dose; LLOQ = lower limit of quantification; LS = least squares; NE=not estimable. PP = per protocol; ULOQ = upper limit of quantification.

Based on PsVNA by Duke University Medical Center Laboratory.

Antibody values reported as below the LLOQ are replaced by 0.5 × LLOQ. Values greater than ULOQ are replaced by the ULOQ if actual values are not available.

100 ug mRNA-1273 group includes young adults (18-25 years of age) from COVE.

* 95% CI is calculated based on the t-distribution of the log-transformed values or the difference in the log-transformed values for GMT and GMFR, respectively, then back-transformed to the original scale for presentation.
†The log-transformed antibody levels are analyzed using an ANCOVA model with the group variable (children in KidCOVE and young adults in COVE) as fixed effect. The resulting LS means, difference of LS means, and 95% CI are back-transformed to the original scale for presentation.
¶95% CI is calculated using the Clopper-Pearson method.
‖95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Table S13. Analysis of Neutralizing Antibody Titers and Seroresponse Rate at Day 57 by Pseudovirus Neutralization Assay (ID_{50}) in Children 6−23 Months in Part 1 Per-protocol Immunogenicity Subset

	6 months to < 2 Years mRNA-1273 25 µg N = 98	18 to ≤ 25 Years mRNA-1273 100 µg N = 295
Baseline GMT (95% CI)	9.6 (9.3-9.9)	9.3 (9.2-9.4)
GMT (95% CI) at Day 57*	1782.6 (1542.0-2060.7)	1299.9 (1170.6-1443.4)
GMFR (95% CI)* at Day 57 from baseline	188.5 (161.9- 219.4)	140.0 (126.1-155.4)
GMR (children vs 18-25 years; model based) (95% CI)†	1.4 (1.1-1.7)	
Participants achieving seroresponse, n (%)§ at Day 57	96/96 (100)	292/295 (99.0)
95% CI¶	96.2-100.0	97.1-99.8
Difference in seroresponse rate (children vs 18-25 years), % (95% CI)‖	1.0 (-2.8-3.0)	

ANCOVA = analysis of covariance; CI = confidence interval; GMFR = geometric mean fold ratio; GMR = geometric mean ratio; GMT = geometric mean titer (noted as observed or model based, which is estimated by geometric least squares mean); ID50 = 50% inhibitory dose; LLOQ = lower limit of quantification; LS = least squares; PP = per protocol; ULOQ = upper limit of quantification.
Based on PsVNA by Duke University Medical Center Laboratory.
Antibody values reported as below the LLOQ are replaced by 0.5 × LLOQ. Values greater than ULOQ are replaced by the ULOQ if actual values are not available.
100 ug mRNA-1273 group includes young adults (18 to 25 years of age) from COVE.
*95% CI is calculated based on the t-distribution of the log-transformed values or the difference in the log-transformed values for GMT and GMFR, respectively, then back-transformed to the original scale for presentation.
† The log-transformed antibody levels are analyzed using an ANCOVA model with the group variable (children in KidCOVE and young adults in COVE) as fixed effect. The resulting LS means, difference of LS means, and 95% CI are back-transformed to the original scale for presentation.
§Seroresponse at a participant level is defined as a change from below the LLOQ to equal or above 4 × LLOQ, or at least a 4-fold rise if baseline is equal to or above the LLOQ. Percentages are based on the number of participants with non-missing data at baseline and the corresponding timepoint.
¶95% CI is calculated using the Clopper-Pearson method.
‖95% CI is calculated using the Miettinen-Nurminen (score) confidence limits.

Table S14. Solicited Local Adverse Reactions in Children 2−5 Years in Part 2 Solicited Safety Set

Local Adverse Reaction n, %	Injection 1		Injection 2	
	Placebo N=970	mRNA-1273 N=2957	Placebo N=9598	mRNA-1273 N=2938
Solicited, N1	970	2957	959	2938
Solicited, any	641 (66.1)	2332 (78.9)	603 (62.9)	2478 (84.3)
Grade 1	463 (47.7)	1629 (55.1)	448 (46.7)	1377 (46.9)
Grade 2	149 (15.4)	612 (20.7)	142 (14.8)	934 (31.8)
Grade 3	27 (2.8)	87 (2.9)	13 (1.4)	160 (5.4)
Grade 4	2 (0.2)	4 (0.1)	0	7 (0.2)
Any Local, N1	970	2956	959	2938
Local, any	407 (42.0)	1874 (63.4)	404 (42.1)	2157 (73.4)
Grade 1	388 (40.0)	1642 (55.5)	390 (40.7)	1691 (57.6)
Grade 2	15 (1.5)	209 (7.1)	14 (1.5)	432 (14.7)
Grade 3	4 (0.4)	23 (0.8)	0	34 (1.2)
Grade 4	0	0	0	0
Pain, N1	970	2954	959	2938
Pain, any	382 (39.4)	1813 (61.4)	395 (41.2)	2099 (71.4)
Grade 1	370 (38.1)	1663 (56.3)	386 (40.3)	1734 (59.0)
Grade 2	12 (1.2)	146 (4.9)	9 (0.9)	354 (12.0)
Grade 3	0	4 (0.1)	0	11 (0.4)
Erythema, N1	970	2955	959	2938
Erythema, any	14 (1.4)	164 (5.5)	15 (1.6)	259 (8.8)
Grade 1	9 (0.9)	110 (3.7)	13 (1.4)	176 (6.0)
Grade 2	2 (0.2)	42 (1.4)	2 (0.2)	71 (2.4)
Grade 3	3 (0.3)	12 (0.4)	0	12 (0.4)
Swelling (Hardness), N1	970	2955	959	2938
Swelling (Hardness), any	17 (1.8)	134 (4.5)	11 (1.1)	240 (8.2)
Grade 1	15 (1.5)	84 (2.8)	11 (1.1)	167 (5.7)
Grade 2	0	40 (1.4)	0	60 (2.0)
Grade 3	2 (0.2)	10 (0.3)	0	13 (0.4)
Axillary Swelling*, N1	970	2954	959	2938
Axillary Swelling, any	56 (5.8)	205 (6.9)	31 (3.2)	267 (9.1)
Grade 1	55 (5.7)	194 (6.6)	28 (2.9)	247 (8.4)
Grade 2	1 (0.1)	11 (0.4)	3 (0.3)	19 (0.6)
Grade 3	0	0	0	1 (<0.1)

*Axillary (or Groin) Swelling or Tenderness. N1 = Number of exposed participants who submitted any data for the event. Any = Grade 1 or higher. Percentages are based on N1.
Pain is injection site pain. Toxicity grade for injection site erythema (redness) or swelling (hardness) is defined as: grade 1=25-50 mm; grade 2=51-100 mm; grade 3=> 100 mm; grade 4=necrosis or exfoliative dermatitis. Toxicity grade for injection site pain and for axillary (underarm or groin) swelling or tenderness is defined as: grade 1=no interference with activity; grade 2=some interference with activity; grade 3=prevents daily activity; grade 4=emergency room visit or hospitalization. Data cutoff date: February 21st, 2022

Table S15. Solicited Local and Systemic Adverse Reactions in Children 6−23 Months in Part 2 Solicited Safety Set

Local Adverse Reaction n, %	Injection 1		Injection 2	
	Placebo N=582	mRNA-1273 25 µg N=1746	Placebo N=526	mRNA-1273 25 µg N=1596
Solicited, N1	582	1746	526	1596
Solicited, any	460 (79.0)	1469 (84.1)	381 (72.4)	1329 (83.3)
Grade 1	323 (55.5)	979 (56.1)	267 (50.8)	776 (48.6)
Grade 2	124 (21.3)	436 (25.0)	102 (19.4)	484 (30.3)
Grade 3	12 (2.1)	53 (3.0)	12 (2.3)	66 (4.2)
Grade 4	1 (0.2)	1 (<0.1)	0	3 (0.2)
Any Local, N1	582	1745	526	1596
Local, any	193 (33.2)	775 (44.4)	159 (30.2)	868 (54.4)
Grade 1	187 (32.1)	701 (40.2)	152 (28.9)	720 (45.1)
Grade 2	4 (0.7)	65 (3.7)	7 (1.3)	126 (7.8)
Grade 3	2 (0.3)	9 (0.5)	0	22 (1.4)
Grade 4	0	0	0	0
Pain, N1	582	1744	526	1596
Pain, any	175 (30.1)	652 (37.4)	135 (25.7)	738 (46.2)
Grade 1	174 (29.9)	636 (36.5)	132 (25.1)	701 (43.9)
Grade 2	1 (0.2)	16 (0.9)	3 (0.6)	37 (2.3)
Grade 3	0	0	0	0
Erythema, N1	582	1744	526	1596
Erythema, any	24 (4.1)	150 (8.6)	20 (3.8)	215 (13.5)
Grade 1	19 (3.3)	110 (6.3)	16 (3.0)	136 (8.5)
Grade 2	3 (0.5)	35 (2.0)	4 (0.8)	66 (4.1)
Grade 3	2 (0.3)	5 (0.3)	0	13 (0.9)
Swelling (Hardness), N1	582	1744	526	1596
Swelling (Hardness), any	15 (2.6)	146 (8.4)	11 (2.1)	243 (15.3)
Grade 1	15 (2.6)	113 (6.5)	10 (1.9)	167 (10.5)
Grade 2	0	28 (1.6)	1 (0.2)	62 (3.9)
Grade 3	0	5 (0.3)	0	14 (0.9)
Axillary Swelling*, N1	582	1743	526	1596
Axillary Swelling*, any	26 (4.5)	102 (5.9)	28 (5.3)	148 (9.3)
Grade 1	26 (4.5)	101 (5.8)	28 (5.3)	146 (9.1)
Grade 2	0	1 (<0.1)	0	2 (0.1)
Grade 3	0	0	0	0
Any systemic, N1	582	1745	526	1596
Systemic, any	421 (72.3)	1334 (76.4)	350 (66.5)	1174 (73.6)
Grade 1	288 (49.5)	891 (51.1)	238 (45.2)	711 (44.5)
Grade 2	122 (21.0)	397 (22.8)	100 (19.0)	416 (26.1)
Grade 3	10 (1.7)	45 (2.6)	12 (2.3)	44 (2.8)
Grade 4	1 (0.2)	1 (<0.1)	0	3 (0.2)
Fever, N1	582	1743	526	1594
Fever, any	49 (8.4)	191 (11.0)	44 (8.4)	232 (14.6)
Grade 1	27 (4.6)	96 (5.5)	19 (3.6)	122 (7.7)
Grade 2	18 (3.1)	83 (4.8)	7 (1.3)	69 (4.3)
Grade 3	3 (0.5)	11 (0.6)	18 (3.4)	38 (2.4)
Grade 4	1 (0.2)	1 (<0.1)	0	3 (0.2)
Irritability/Crying, N1	581	1737	525	1589
Irritability/Crying, any	361 (62.1)	1175 (67.6)	307 (58.5)	1021 (64.3)
Grade 1	248 (42.7)	815 (46.9)	214 (40.8)	647 (40.7)
Grade 2	107 (18.4)	336 (19.3)	88 (16.8)	349 (22.0)

Grade 3	6 (1.0)	24 (1.4)	5 (1.0)	25 (1.6)
Sleepiness, N1	581	1739	525	1589
Sleepiness, any	217 (37.3)	645 (37.1)	175 (33.3)	558 (35.1)
Grade 1	211 (36.3)	624 (35.9)	168 (32.0)	546 (34.4)
Grade 2	5 (0.9)	17 (1.0)	6 (1.1)	11 (0.7)
Grade 3	1 (0.2)	4 (0.2)	1 (0.2)	1 (<0.1)
Loss of Appetite, N1	581	1737	525	1589
Loss of Appetite, any	152 (26.2)	524 (30.2)	132 (25.1)	510 (32.1)
Grade 1	135 (23.2)	456 (26.3)	116 (22.1)	438 (27.6)
Grade 2	16 (2.8)	58 (3.3)	14 (2.7)	56 (3.5)
Grade 3	1 (0.2)	10 (0.6)	2 (0.4)	16 (1.0)

*Axillary (or Groin) Swelling or Tenderness. N1 = Number of exposed participants who submitted any data for the event. Any = Grade 1 or higher. Percentages are based on N1.
Pain is injection site pain. Toxicity grade for injection site erythema (redness) or swelling (hardness) is defined as: grade 1=25-50 mm; grade 2=51-100 mm; grade 3=> 100 mm; grade 4=necrosis or exfoliative dermatitis. Toxicity grade for injection site pain and for axillary (underarm or groin) swelling or tenderness is defined as: grade 1=no interference with activity; grade 2=some interference with activity; grade 3=prevents daily activity; grade 4=emergency room visit or hospitalization. Toxicity grade for Fever for children age 6 to ≤36 months is defined as: G1 = 38 —38.4 C; G2 = 38.5 —39.5 C; G3 = 39 —40 C; G4 = > 40 C. Data cutoff date: February 21st, 2022.

Table S16. Summary Duration (Days) of Local and Systemic Adverse Reactions in Children 2−5 Years Following Injections 1 and 2 in Part 2 Solicited Safety Set

	Injection 1			Injection 2		
Duration days	**Placebo**	**mRNA-1273 25 µg**	**Total**	**Placebo**	**mRNA-1273 25 µg**	**Total**
	N=970	**N=2957**	**N=3927**	**N=959**	**N=2938**	**N=3897**
Any solicited, n	641	2332	2973	603	2478	3081
Mean days (SD)	3.0 (3.1)	2.9 (2.3)	3.0 (2.5)	2.6 (2.1)	3.1 (2.1)	3.0 (2.1)
Median days (IQR)	2.0 (1.0-4.0)	2.0 (1.0-4.0)	2.0 (1.0-4.0)	2.0 (1.0-3,0)	2.0 (1.0-4,0)	2.0 (1.0-4,0)
Any local AR, n	407	1874	2281	404	2157	2561
Mean days (SD)	1.8 (1.9)	2.1 (1.6)	2.0 (1.7)	1.6 (1.1)	2.3 (1.6)	2.2 (1.5)
Median days (IQR)	1.0 (1.0-2.0)	2.0 (1.0-3.0)	1.0(1.0-2.0)	1.0 (1.0-2,0)	2.0 (1.0-3,0)	2.0 (1.0-3,0)
Pain, n	382	1813	2195	395	2099	2494
Mean days (SD)	1.7 (1.8	2.0 (1.3)	1.9 (1.4)	1.5 (1.0)	2.2 (1.3)	2.1 (1.3)
Median days (IQR)	1.0 (1.0-2.0)	2.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2,0)	2.0 (1.0-3,0)	2.0 (1.0-3,0)
Erythema (redness), n	14	164	178	15	259	274
Mean days (SD)	1.0 (0)	2.0 (1.8)	1.9 (1.8)	1.4 (0.7)	1.7 (1.0)	1.7 (1.0)
Median days (IQR)	1.0 (1.0-1,0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)
Swelling (hardness), n	17	134	151	11	240	251
Mean days (SD)	1.1 (0.2)	1.9 (1.7)	1.8 (1.6)	1.2 (0.4)	2.0 (1.5)	1.9 (1.5)
Median days (IQR)	1.0 (1.0-1,0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)	1.0 (1.0-1,0)	1.0 (1.0-3,0)	1.0 (1.0-3,0)
Axillary (or groin) swelling/tenderness (n)	56	205	261	31	267	298
Mean days (SD)	1.7 (1.3)	2.0 (2.2)	1.9 (2.1)	1.5 (1.1)	2.4 (2.2)	2.3 (2.2)
Median days (IQR)	1.0 (1.0-2,0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)	1.0 (1.0-3,0)	1.0 (1.0-3,0)
Any systemic AR, n	488	1595	2083	428	1814	2242
Mean days (SD)	2.9 (3.0)	2.6 (2.7)	2.7 (2.5)	2.5 (2.1)	2.6 (2.1)	2.6 (2.1)
Median days (IQR)	2.0 (1.0-4,0)	2.0 (1.0-4,0)	2.0 (1.0-4,0)	1.0 (1.0-3,0)	2.0 (1.0-3,0)	2.0 (1.0-3,0)
Fever, n	58	261	319	63	498	561
Mean days (SD)	2.4 (3.2)	1.6 (1.3)	1.8 (1.8)	1.8 (1.3)	1.5 (1.2)	1.6 (1.2)
Median days (IQR)	1.0 (1.0-3,0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)
Headache, n	78	232	310	51	310	361
Mean days (SD)	1.6 (1.3)	1.7 (1.4)	1.6 (1.4)	1.5 (1.1)	1.7 (1.4)	1.7 (1.4)
Median days (IQR)	1.0 (1.0-2,0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)
Fatigue, n	236	807	1043	185	956	1141
Mean days (SD)	2.5 (2.9)	2.2 (2.0)	2.3 (2.2)	2.1 (1.9)	2.2 (1.8)	2.2 (1.8)
Median days (IQR)	1.0 (1.0-3,0)	1.0 (1.0-3,0)	1.0 (1.0-3,0)	1.0 (1.0-3,0)	1.0 (1.0-3,0)	1.0 (1.0-3,0)
Myalgia, n	60	200	260	47	310	357
Mean days (SD)	1.3 (0.9)	1.7 (1.4)	1.6 (1.3)	1.6 (1.4)	1.5 (1.0)	1.5 (1.1)
Median days (IQR)	1.0 (1.0-1,0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)	1.0 (1.0-1,0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)
Arthralgia, n	32	124	156	28	168	196
Mean days (SD)	1.5 (1.4)	1.6 (1.4)	1.6 (1.4)	1.9 (1.4)	1.4 (1.0)	1.5 (1.0)
Median days (IQR)	1.0 (1.0-1,0)	1.0 (1.0-1,0)	1.0 (1.0-1,0)	1.0 (1.0-2.5)	1.0 (1.0-1,0)	1.0 (1.0-1,0)
Nausea/vomiting, n	50	137	187	30	194	224
Mean days (SD)	1.5 (1.3)	1.5 (1.1)	1.5 (1.2)	1.3 (0.8)	1.6 (1.2)	1.6 (1.2)
Median days (IQR)	1.0 (1.0-2,0)	1.0 (1.0-1,0)	1.0 (1.0-1,0)	1.0 (1.0-1,0)	1.0 (1.0-1,0)	1.0 (1.0-1,0)
Chills, n	40	129	169	31	245	276
Mean days (SD)	1.7 (1.4)	1.5 (1.4)	1.5 (1.4)	1.7 (2.1)	1.3 (0.8)	1.4 (1.0)
Median days (IQR)	1.0 (1.0-2,0)	1.0 (1.0-1,0)	1.0 (1.0-1,0)	1.0 (1.0-3,0)	1.0 (1.0-4,0)	1.0 (1.0-4,0)
Irritability/Crying	163	513	676	148	523	671
Mean days (SD)	2.8 (2.8)	2.6 (2.3)	2.6 (2.4)	1.7 (2.1)	1.3 (0.8)	1.4 (1.0)
Median days (IQR)	1.0 (1.0-4.0)	1.0 (1.0-4,0)	1.0 (1.0-4,0)	1.0 (1.0-3,0)	2.0 (1.0-4,0)	2.0 (1.0-4,0)
Sleepiness	92	285	377	89	347	436
Mean days (SD)	2.5 (2.3)	2.1 (2.0)	2.2 (2.0)	2.1 (1.8)	2.0 (1.6)	2.0 (1.7)
Median days (IQR)	1.0 (1.0-3,0)	1.0 (1.0-3,0)	1.0 (1.0-3,0)	1.0 (1.0-3,0)	1.0 (1.0-2,0)	1.0 (1.0-2,0)

Loss of Appetite	71	225	296	69	294	363
Mean days (SD)	2.5 (2.8)	2.3 (2.0)	2.3 (2.2	2.2 (2.1)	2.4 (2.1)	2.4 (2.1)
Median days (IQR)	1.0 (1.0-3,0)	1.0 (1.0-3,0)	1.0 (1.0-3,0)	1.0 (1.0-2,0)	2.0 (1.0-3,0)	1.0 (1.0-3,0)

AR, adverse reaction; IQR-interquartile range; N, number of exposed participants who reported the event on any day within 7 days of the first injection. n = Number of exposed participants who reported the event on any day within 7 days of the first injection.
Duration is calculated as the last day — the first day + 1 when the solicited adverse reaction was reported starting within the 7 days of injection. If the solicited adverse reaction continued beyond 7 days, the days after 7 days were included. Pain for children ages 6 to ≤36 months is injection-site pain or tenderness, and for 37 months to <12 years is injection-site pain. The number of days which is higher for solicited events after either the first or the second injection is summarized. Data cut-off date: February 21, 2022.

Table S17. Summary Duration (Days) of Local and Systemic Adverse Reactions in Children 6−23 Months Following Injections 1 and 2 in Part 2 Solicited Safety Set

	Injection 1			Injection 2		
Duration days 6 months-<2 years	**Placebo N=582**	**mRNA-1273 25 µg N=1746**	**Total N=2328**	**Placebo N=526**	**mRNA-1273 25 µg N=1596**	**Total N=2122**
Any solicited, n	460	1469	1929	381	1329	1710
Mean days (SD)	3.6 (2.9)	3.9 (3.3)	3.8 (3.2)	3.4 (2.6)	3.8 (3.3)	3.7 (3.2)
Median days (IQR)	3.0 (1.0-5.0)	3.0 (1.0-6.0)	3.0 (1.0-6.0)	3.0 (1.0-5.0)	3.0 (1.0-5.0)	3.0 (1.0-5.0)
Any local, n	193	775	968	159	868	1027
Mean days (SD)	1.6 (1.1)	2.0 (2.3)	2.0 (2.1)	1.7 (1.2)	2.4 (2.9)	2.3 (2.7)
Median days (IQR)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	2.0 (1.0-3.0)	1.0 (1.0-3.0)
Pain, n	175	652	827	135	738	873
Mean days (SD)	1.4 (0.8)	1.6 (1.1)	1.6 (1.1)	1.7 (1.1)	1.9 (1.3)	1.9 (1.3)
Median days (IQR)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)
Erythema (redness), n	24	150	174	20	215	235
Mean days (SD)	1.2 (0.7)	1.6 (1.5)	1.5 (1.4)	1.1 (0.2)	1.6 (1.2)	1.5 (1.2)
Median days (IQR)	1.0 (1.0-1.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-1.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)
Swelling (hardness), n	15	146	161	11	243	254
Mean days (SD)	1.4 (1.1)	1.9 (1.8)	1.9 (1.7)	1.5 (0.9)	2.1 (1.5)	2.1 (1.4)
Median days (IQR)	1.0 (1.0-1.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	2.0 (1.0-3.0)	1.5 (1.0-3.0)
Axillary (or groin) swelling/tenderness, n	26	102	128	28	148	176
Mean days (SD)	2.0 (1.8)	3.1 (4.5)	2.9 (4.2)	1.7 (1.2)	3.6 (5.4)	3.3 (5.0)
Median days (IQR)	1.0 (1.0-3.0)	1.0 (1.0-3.0)	1.0 (1.0-3.0)	1.0 (1.0-2.0)	2.0 (1.0-4.0)	1.0 (1.0-3.5)
Any systemic, n	421	1334	1755	350	1174	1524
Mean days (SD)	3.6 (2.9)	3.7 (3.1)	3.6 (3.0)	3.4 (2.6)	3.4 (2.9)	3.4 (2.8)
Median days (IQR)	3.0 (1.0-5.0)	3.0 (1.0-6.0)	3.0 (1.0-6.0)	3.0 (1.0-5.0)	3.0 (1.0-5.0)	3.0 (1.0-5.0)
Fever, n	49	191	240	44	232	276
Mean days (SD)	1.6 (1.1)	1.6 (1.2)	1.6 (1.2)	1.7 (1.1)	1.7 (1.5)	1.7 (1.4)
Median days (IQR)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)
Irritability/Crying	361	1175	1536	307	1021	1328
Mean days (SD)	3.4 (3.0)	3.3 (3.1)	3.3 (3.0)	2.9 (2.5)	3.1 (2.4)	3.0 (2.4)
Median days (IQR)	2.0 (1.0-5.0)	2.0 (1.0-5.0)	2.0 (1.0-5.0)	2.0 (1.0-4.0)	2.0 (1.0-4.0)	2.0 (1.0-4.0)
Sleepiness	217	645	862	175	558	733
Mean days (SD)	2.1 (1.8)	2.1 (1.7)	2.1 (1.7)	2.2 (1.8)	2.2 (1.8)	2.2 (1.8)
Median days (IQR)	1.0 (1.0-3.0)	1.0 (1.0-3.0)	1.0 (1.0-3.0)	1.0 (1.0-3.0)	1.0 (1.0-3.0)	1.0 (1.0-3.0)
Loss of Appetite	152	524	676	132	510	642
Mean days (SD)	2.4 (2.2)	2.2 (1.9)	2.3 (2.0)	2.7 (2.3)	2.5 (2.9)	2.6 (2.8)
Median days (IQR)	1.0 (1.0-3.0)	1.0 (1.0-3.0)	1.0 (1.0-3.0)	2.0 (1.0-4.0)	1.0 (1.0-3.0)	1.0 (1.0-3.0)

AR, adverse reaction; IQR, interquartile range; N, number of exposed participants who reported the event on any day within 7 days of the first injection. Duration is calculated as the last day — the first day + 1 when the solicited adverse reaction was reported starting within the 7 days of injection. If the solicited adverse reaction continues beyond 7 days, the days after 7 days are included. The number of days which is higher with solicited events after either the first or the second injection is summarized. Data cut-off date: February 21, 2022.

Table S18. Solicited Systemic Adverse Reactions in Children 37 Months-5 Years in Part 2 Solicited Safety Set

Systemic Adverse Reactions n (%)	Injection 1		Injection 2	
	Placebo N=650	mRNA-1273 N=2013	Placebo N=629	mRNA-1273 N=1975
Any Systemic AR, N1	650	2013	629	1975
Systemic AR, any	290 (44.6)	983 (48.8)	234 (37.2)	1163 (58.9)
Grade 1	176 (27.1)	613 (30.5)	149 (23.7)	559 (28.3)
Grade 2	99 (15.2)	322 (16.0)	74 (11.8)	500 (25.3)
Grade 3	14 (2.2)	47 (2.3)	11 (1.7)	100 (5.1)
Grade 4	1 (0.2)	1 (<0.1)	0	4 (0.2)
Fever, N1	650	2013	627	1974
Fever, any	33 (5.1)	155 (7.7)	28 (4.5)	316 (16.0)
Grade 1	20 (3.1)	93 (4.6)	19 (3.0)	159 (8.1)
Grade 2	8 (1.2)	38 (1.9)	7 (1.1)	95 (4.8)
Grade 3	4 (0.6)	23 (1.1)	2 (0.3)	58 (2.9)
Grade 4	1 (0.2)	1 (<0.1)	0	4 (0.2)†
Headache, N1	650	2013	629	1975
Headache	78 (12.0)	232 (11.5)	51 (8.1)	310 (15.7)
Grade 1	66 (10.2)	181 (9.0)	43 (6.8)	193 (9.8)
Grade 2	10 (1.5)	46 (2.3)	7 (1.1)	109 (5.5)
Grade 3	2 (0.3)	5 (0.2)	1 (0.2)	8 (0.4)
Fatigue, N1	650	2013	629	1975
Fatigue	236 (36.3)	807 (40.1)	185 (29.4)	956 (48.4)
Grade 1	138 (21.2)	503 (25.0)	113 (18.0)	476 (24.1)
Grade 2	87 (13.4)	283 (14.1)	64 (10.2)	435 (22.0)
Grade 3	11 (1.7)	21 (1.0)	8 (1.3)	45 (2.3)
Myalgia, N1	650	2013	629	1975
Myalgia	60 (9.2)	200 (9.9)	47 (7.5)	310 (15.7)
Grade 1	46 (7.1)	138 (6.9)	30 (4.8)	191 (9.7)
Grade 2	12 (1.8)	57 (2.8)	14 (2.2)	110 (5.6)
Grade 3	2 (0.3)	5 (0.2)	3 (0.5)	9 (0.5)
Arthralgia, N1	650	2013	629	1975
Arthralgia	32 (4.9)	124 (6.2)	28 (4.5)	168 (8.5)
Grade 1	28 (4.3)	101 (5.0)	18 (2.9)	118 (6.0)
Grade 2	3 (0.5)	21 (1.0)	10 (1.6)	47 (2.4)
Grade 3	1 (0.2)	2 (<0.1)	0	3 (0.2)
Nausea/vomiting, N1	650	2013	629	1975
Nausea /vomiting	50 (7.7)	137 (6.8)	30 (4.8)	194 (9.8)
Grade 1	38 (5.8)	113 (5.6)	25 (4.0)	152 (7.7)
Grade 2	10 (1.5)	17 (0.8)	5 (0.8)	36 (1.8)
Grade 3	2 (0.3)	7 (0.3)	0	6 (0.3)
Chills, N1	650	2013	629	1975
Chills	40 (6.2)	129 (6.4)	31 (4.9)	245 (12.4)
Grade 1	29 (4.5)	99 (4.9)	21 (3.3)	164 (8.3)
Grade 2	11 (1.7)	29 (1.4)	8 (1.3)	77 (3.9)
Grade 3	0	1 (<0.1)	2 (0.3)	4 (0.2)

*= Axillary (or Groin) Swelling or Tenderness. N1 = Number of exposed participants who submitted any data for the event. Any = Grade 1 or higher. Percentages are based on N1. Toxicity grade for solicited systemic adverse reactions other than fever is defined as: grade 1 = no interference with activity (or, for nausea/vomiting: 1 2 episodes/24 hours); grade 2 = some interference with activity (or, for nausea/vomiting: > 2 episodes/24 hours); grade 3 = prevents daily activity; grade 4 = emergency room visit or hospitalization. Protocol-defined toxicity grades for fever in participants 37 months to <6 years of age were: grade 1 = 38°C to 38.4°C, grade 2 = 38.5°C to 38.9°C, grade 3 = 39°C to 40°C, and grade 4 > 40°C. †Fever was reported in error in two participants as none recorded any elevated temperature, as determined by the investigator Data cutoff date: February 21, 2022.

Table S19. Solicited Systemic Adverse Reactions in Children 24-36-Months in Part 2 Solicited Safety Set

Systemic Adverse Reactions n (%)	Injection 1		Injection 2	
	Placebo N=320	mRNA-1273 N=944	Placebo N=330	mRNA-1273 N=963
Any Systemic, N1	320	942	330	963
Systemic, any	198 (61.9)	612 (65.0)	194 (58.8)	651 (67.6)
Grade 1	142 (44.4)	423 (44.9)	133 (40.3)	401 (41.6)
Grade 2	46 (14.4)	168 (17.8)	59 (17.9)	219 (22.7)
Grade 3	9 (2.8)	18 (1.9)	2 (0.6)	28 (2.9)
Grade 4	1 (0.3)	3 (0.3)	0	3 (0.3)
Fever, N1	320	942	330	962
Fever	25 (7.8)	106 (11.3)	35 (10.6)	182 (18.9)
Grade 1	9 (2.8)	64 (6.8)	15 (4.5)	89 (9.3)
Grade 2	12 (3.8)	36 (3.8)	20 (6.1)	78 (8.1)
Grade 3	3 (0.9)	3 (0.3)	0	12 (1.2)
Grade 4	1 (0.3)	3 (0.3)†	0	3 (0.3)
Irritability/Crying,N1	319	941	330	963
Irritability/Crying	163 (51.1)	513 (54.5)	148 (44.8)	523 (54.3)
Grade 1	122 (38.2)	366 (38.9)	108 (32.7)	347 (36.0)
Grade 2	35 (11.0)	135 (14.3)	38 (11.5)	166 (17.2)
Grade 3	6 (1.9)	12 (1.3)	2 (0.6)	10 (1.0)
Sleepiness, N1	319	941	330	963
Sleepiness	92 (28.8)	285 (30.3)	89 (27.0)	347 (36.0)
Grade 1	88 (27.6)	275 (29.2)	89 (27.0)	334 (34.7)
Grade 2	4 (1.3)	8 (0.9)	0	12 (1.2)
Grade 3	0	2 (0.2)	0	1 (0.1)
Loss of Appetite, N1	319	941	330	963
Loss of Appetite	71 (22.3)	225 (23.9)	69 (20.9)	294 (30.5)
Grade 1	61 (19.1)	190 (20.2)	61 (18.5)	243 (25.2)
Grade 2	9 (2.8)	28 (3.0)	8 (2.4)	43 (4.5)
Grade 3	1 (0.3)	7 (0.7)	0	8 (0.8)

*= Axillary (or Groin) Swelling or Tenderness. N1 = Number of exposed participants who submitted any data for the event. Any = Grade 1 or higher. Percentages are based on N1.

Toxicity grade for solicited systemic adverse reactions other than fever is defined as: grade 1 = no interference with activity (or, for nausea/vomiting: 1-2 episodes/24 hours); grade 2 = some interference with activity (or, for nausea/vomiting: > 2 episodes/24 hours); grade 3 = prevents daily activity; grade 4 = emergency room visit or hospitalization. Protocol-defined toxicity grades for fever in participants 2 years to ≤36 months were: grade 1 = 38°C to 38.5°C, grade 2 = 38.6°C to 39.5°C, grade 3 = 39.6°C to 40°C, and grade 4 > 40.0°C. †Fever was reported in error in two participants as none recorded any elevated temperature, as determined by the investigator. Data cutoff date: February 21, 2022.

Table S20. Summary of Participants Reporting Fevers >40°C in Children 2−5 Years and 6−23 Months in Part 2

Case #	Injection #	Start day of any fever	Duration of any fever (days)	Age	Treatment	SARS-COV-2 status at baseline	Reported concurrent AE
2-5 years							
1	1	D4	2	2 y	mRNA-1273	Positive	No
2	1	D5	2	2 y	Placebo	Negative	SARS-CoV-2 infection
3	1	D3	3	2 y	mRNA-1273	Negative	No
4	1	D2	2	3 y	Placebo	Negative	No
5	1	D3	3	2 y	mRNA-1273	Negative	URI
6	2	D2	2	2 y	mRNA-1273	Positive	No
7	2	D2	4	4 y	mRNA-1273	Negative	Croup
8	2	D1	4	2 y	mRNA-1273	Negative	Bilateral viral pneumonia
9	2	D3	1	3 y	mRNA-1273	Negative	No
10	2	D2	2	2 y	mRNA-1273	Negative	No
6-23 months							
1	1	D6	6	1 y	Placebo	Negative	Viral rash
2	1	D4	4	1 y	mRNA-1273	Negative	No
3	2	D2	4	1 y	mRNA-1273	Negative	URI
4	2	D4	7	1 y	mRNA-1273	Negative	URI (twin of #5)
5	2	D4	3	1 y	mRNA-1273	Negative	URI (twin of #4)

D=day; y=year; SARS-CoV-2 = severe acute respiratory syndrome coronavirus-2; URI = upper respiratory tract infection.

Table S21. Summary of Unsolicited Adverse Events <28 Days in Children 2−5 Years and 6−23 Months in Part 2 Safety Set

n (%)	2-5 years		6-23 months	
	Placebo	mRNA-1273 25 µg	Placebo	mRNA-1273 25 µg
	N=1007	N=3031	N=589	N=1911
Unsolicited AEs regardless of relationship to study vaccination				
All	378 (37.5)	1212 (40.0)	284 (48.2)	869 (49.3)
Serious	1 (<0.1)	4 (0.1)	0	8 (0.5)*
Fatal	0	0	0	0
Medically attended	221 (21.9)	662 (21.8)	161 (27.3)	486 (27.6)
Leading to discontinuation from study vaccine	0	0	1 (0.2)	1 (<0.1)
Leading to discontinuation from study	0	0	1 (0.2)	0
Severe	9 (0.9)	22 (0.7)	4 (0.7)	21 (1.2)
Non-serious	378 (37.5)	1211 (40.0)	363 (15.4)	315 (16.5)
Severe	9 (0.9)	21 (0.7)	15 (0.6)	14 (0.7)
Special interest (AESI)	1 (<0.1)	5 (0.2)	0	3 (0.2)
MIS-C	0	0	0	0
Other	1 (<0.1)†	5 (0.2)§	0	3 (0.2)¶
Unsolicited AEs related to study vaccination				
All	80 (7.9)	286 (9.4)	71 (12.1)	292 (16.6)
Serious	0	0	0	1 (<0.1)*
Fatal	0	0	0	0
Medically attended	3 (0.3)	30 (1.0)	3 (0.5)	23 (1.3)
Leading to discontinuation from study vaccine	0	0	0	1 (<0.1)
Leading to discontinuation from study	0	0	0	0
Severe	8 (0.8)	18 (0.6)	3 (0.5)	12 (0.7)
Non-serious	80 (7.9)	286 (9.4)	71 (12.1)	292 (16.6)
Severe	8 (0.8)	18 (0.6)	3 (0.5)	12 (0.7)
Special interest (AESI)	1 (<0.1)	2 (<0.1)	0	2 (0.1)
MIS-C	0	0	0	0
Other	1 (<0.1)†	2 (<0.1)†	0	2 (0.1)†

AE, adverse event; AESI, adverse event of special interest; MIS-C, multisystem inflammatory syndrome in children. An AE is defined as any event not present before exposure to study vaccination or any event already present that worsens in intensity or frequency after exposure. Percentages are based on the number of participants in the safety set. Solicited adverse reactions with toxicity grade = 0 that lasted beyond day 7 or started after day 7 are not included in this table. *1 (<0.1%) participant (1-yr-old female) experienced grade 3 SAEs of fever (103.1°F) and febrile convulsion 2 days after the first dose and also developed a rash 2 days later suggesting a viral etiology of the fever, considered not related to study vaccination and 1 SAE considered related of pyrexia occurred. The child was able to receive dose 2 without any events. †Two nonserious AESI grade 1 events of ageusia and anosmia (3-year-old female), not considered study vaccination related and a study vaccination related grade 3 event of Henoch-Schönlein purpura (3-year-old female). §Five AESIs reported in 5 participants including non-study vaccination related AESIs of grade 1 food allergy (2-year-old male), serious grade 1 event of seizure (4-year-old male), and grade 1 erythema multiforme (3-year-old female), and two events considered vaccination related of grade 1 erythema multiforme (3-year-old male) and one grade 2 chest pain (4-year-old male) ¶3 AESIs including a grade 3 febrile convulsion (1-yr-old male), not considered related to study vaccination that occurred 21 days post-injection 1 and resolved the same day, and 2 AESIs considered related including the above-described SAE of febrile seizure and a grade 1 AESI of liver injury (9-month-old female). After the analysis cutoff date, a 3-year-old participant was diagnosed with MIS-C that started 113 days after placebo injection 2, considered not related by the investigator. The participant had a grade 1 asymptomatic SARS-CoV-2 infection 37 days prior to the onset of symptoms. Five days after onset of MIS-C symptoms, the child was hospitalized then discharged after 4 days with a diagnosis of MIS-C and was recovering with cardiology and rheumatology follow-up pending at time of writing. Data cut-off date: February 21, 2022.

Table S22. Summary of Unsolicited and Severe Adverse Events Reported ≤28 Days in Children 2−5 Years After Any Injection by MedDRA Primary System Organ Class and Preferred Term in Part 2 Safety Set

System Organ Class Preferred Term n (%)	Placebo N=1007		mRNA-1273 25 µg (N=3031)	
	Any	Severe	Any	Severe
Number of participants reporting unsolicited adverse events	378 (37.5)	9 (0.9)	1212 (40.0)	22 (0.7)
Number of unsolicited adverse events	677	11	2009	31
Infections and infestations	245 (24.3)	0	707 (23.3)	2 (<0.1)
Bronchiolitis	2 (0.2)	0	3 (<0.1)	1 (<0.1)
Metapneumovirus infection	1 (<0.1)	0	7 (0.2)	1 (<0.1)
Pneumonia viral	0	0	2 (<0.1)	1 (<0.1)
Metabolism and nutrition disorders	14 (1.4)	0	40 (1.3)	2 (<0.1)
Decreased appetite	14 (1.4)	0	39 (1.3)	2 (<0.1)
Psychiatric disorders	19 (1.9)	2 (0.2)	49 (1.6)	1 (<0.1)
Irritability	16 (1.6)	2 (0.2)	49 (1.6)	1 (<0.1)
Nervous system disorders	14 (1.4)	0	32 (1.1)	1 (<0.1)
Headache	4 (0.4)	0	12 (0.4)	1 (<0.1)
Respiratory, thoracic, and mediastinal disorders	84 (8.3)	0	233 (7.7)	2 (<0.1)
Bronchial hyperreactivity	1 (<0.1)	0	5 (0.2)	1 (<0.1)
Respiratory distress	0	0	1 (<0.1)	1 (<0.1)
Tonsillar hypertrophy	1 (<0.1)	0	1 (<0.1)	1 (<0.1)
Gastrointestinal disorders	47 (4.7)	0	133 (4.4)	1 (<0.1)
Vomiting	14 (1.4)	0	55 (1.8)	1 (<0.1)
Skin and subcutaneous tissue disorders	14 (1.4)	1 (<0.1)	62 (2.0)	0
Henoch-Schonlein purpura	1 (<0.1)	1 (<0.1)	0	0
Musculoskeletal and connective tissue disorders	9 (0.9)	1 (<0.1)	21 (0.7)	2 (<0.1)
Myalgia	2 (0.2)	1 (<0.1)	5 (0.2)	1 (<0.1)
Neck pain	0	0	1 (<0.1)	1 (<0.1)
General disorders and administration site conditions	62 (6.2)	6 (0.6)	248 (8.2)	16 (0.5)
Pyrexia	36 (3.6)	4 (0.4)	95 (3.1)	11 (0.4)
Fatigue	23 (2.3)	3 (0.3)	58 (1.9)	4 (0.1)
Chills	4 (0.4)	0	4 (0.1)	1 (<0.1)
Injection site erythema	2 (0.2)	0	38 (1.3)	1 (<0.1)
Injection site induration	1 (<0.1)	0	15 (0.5)	1 (<0.1)

Covid-19, coronavirus disease 2019; MedDRA, Medical Dictionary for Regulatory Activities.
Percentages are based on the number of safety participants. MedDRA version 23.0. Data cut-off date: February 21, 2022.

Table S23. Summary of Unsolicited and Severe Adverse Events Reported ≤28 Days in Children 6−23 Months After Any Injection by MedDRA Primary System Organ Class and Preferred Term in Part 2 Safety Set

System Organ Class Preferred Term n (%)	Placebo N=589		mRNA-1273 25 µg (N=1761)	
	Any	Severe	Any	Severe
Number of participants reporting unsolicited adverse events	284 (48.2)	4 (0.7)	1153 (49.1)	21 (1.2)
Number of unsolicited adverse events	572	6	1711	25
Infections and infestations	183 (31.1)	1 (0.2)	526 (29.9)	7 (0.4)
Respiratory tract infection viral	2 (0.3)	1 (0.2)	3 (0.2)	1 (<0.1)
Bronchiolitis	2 (0.3)	0	7 (0.4)	1 (<0.1)
Gastroenteritis viral	3 (0.5)	0	12 (0.7)	1 (<0.1)
Hand-foot-and-mouth disease	526 (29.9)	1 (0.2)	27 (1.5)	0
Mastoiditis	0	0	1 (<0.1)	1 (<0.1)
Pneumonia	0	0	3 (0.2)	1 (<0.1)
Respiratory syncytial virus infection	3 (0.5)	0	3 (0.5)	1 (<0.1)
Rhinovirus infection	0	0	9 (0.5)	1 (<0.1)
Immune system disorders	8 (1.4)	0	8 (0.5)	1 (<0.1)
Food allergy	4 (0.7)	0	2 (0.1)	1 (<0.1)
Metabolism and nutrition disorders	26 (4.4)	1 (0.2)	71 (4.0)	4 (0.2)
Decreased appetite	26 (4.4)	1 (0.2)	68 (3.9)	3 (0.2)
Electrolyte imbalance	0	0	1 (<0.1)	1 (<0.1)
Psychiatric disorders	48 (8.1)	1 (0.2)	152 (8.6)	8 (0.5)
Irritability	47 (8.0)	1 (0.2)	151 (8.6)	8 (0.5)
Nervous system disorders	15 (2.5)	0	38 (2.2)	2 (0.1)
Febrile convulsion	0	0	2 (0.1)	2 (0.1)
Respiratory, thoracic and mediastinal disorders	46 (7.8)	0	143 (8.1)	0
Cough	21 (3.6)	0	74 (4.2)	0
Wheezing	0	0	1 (<0.1)	0
Skin and subcutaneous tissue disorders	21 (3.6)	0	52 (3.0)	1 (<0.1)
Urticaria	5 (0.8)	0	7 (0.4)	1 (<0.1)
General disorders and administration site conditions	37 (6.3)	2 (0.3)	147 (8.3)	1 (<0.1)
Pyrexia	31 (5.3)	2 (0.3)	31 (5.3)	1 (<0.1)
Injury, poisoning and procedural complications	10 (1.7)	0	30 (1.7)	1 (<0.1)
Radial head dislocation	1 (0.2)	0	3 (0.2)	1 (<0.1)

Covid-19, coronavirus disease 2019; MedDRA, Medical Dictionary for Regulatory Activities.
Percentages are based on the number of safety participants. MedDRA version 23.0. Data cut-off date: February 21, 2022.

Table S24. Summary of Serious Adverse Events ≤28 Days After Any Injection Regardless of Attribution in Children 2−5 Years and 6−23 Months in Part 2 Safety Set

System Organ Class Preferred Term n (%)	Placebo	mRNA-1273 25 µg
2-5 years	**(N = 995)**	**(N = 3007)**
Number of participants reporting unsolicited serious AEs	1 (<0.1)	4 (0.1)
Number of unsolicited serious adverse events	1	6
Infections and infestations	1 (<0.1)	3 (< 0.1)
Abdominal wall abscess	1 (<0.1)	0
Adenovirus infection	0	1 (< 0.1)
Metapneumovirus infection	0	1 (< 0.1)
Pneumonia viral	0	1 (< 0.1)
Nervous system disorders	0	1 (< 0.1)
Seizure	0	1 (< 0.1)
Respiratory, thoracic and mediastinal disorders	0	1 (<0.1)
Bronchial hyperreactivity	0	1 (< 0.1)
Respiratory distress	0	1 (< 0.1)
6-23 months	**(N = 589)**	**(N = 1761)**
Number of participants reporting unsolicited serious AEs	0	8 (0.5)
Number of unsolicited serious adverse events	0	9
Infections and infestations	0	4 (0.2)
Bronchiolitis	0	1 (< 0.1)
Mastoiditis	0	1 (< 0.1)
Metapneumovirus infection	0	1 (< 0.1)
Rhinovirus infection	0	1 (< 0.1)
Metabolism and nutrition disorders	0	1 (< 0.1)
Electrolyte imbalance	0	1 (< 0.1)
Nervous system disorders	0	2 (0.1)
Febrile convulsion	0	2 (0.1)
General disorders and administration site conditions	0	1 (< 0.1)
Pyrexia	0	1 (< 0.1)
Injury, poisoning and procedural complications	0	1 (< 0.1)
Foreign body in respiratory tract	0	1 (< 0.1)

MedDRA = Medical Dictionary for Regulatory Activities.
Note: Percentages are based on the number of safety participants. MedDRA version 23.0. Data cutoff date: February 21, 2022.

Table S25. Time to Onset of Reported Febrile Seizures in Children 6−23 Months in Safety Set

Age at Enrollment	Sex	Time to Onset	Related per Investigator	Concurrent AEs
17 months	Female	2 days post-injection 1	Yes	Fever to 103.1°F; maculopapular rash on trunk 2 days post event*
16 months	Male	10 days post-injection 2	No	Fever to 102.2°F; maculopapular rash on trunk, urticaria bilateral cheeks, URI, bilateral otitis media
19 months	Male	21 days post-injection 2	No	Fever to 101ºF, diagnosed with Periodic Fever, Aphthous Stomatitis, Pharyngitis, Adenitis Syndrome (PFAPA) after data cut
17 months	Female	66 days post-injection 2	No	Fever to 101.5ºF, considered likely viral by ER physician
ER=emergency room; URI=upper respiratory infection *Post 21 Feb 2022 data cut this child experienced another febrile seizure ~6 weeks after; the first seizure. The child received injection 2 with antipyretics after the event with no additional events reported.				

Table S26. Summary of Unsolicited Adverse Events After Any Injection Throughout the Study

n (%)	2-5 years		6-23 months	
	Placebo	mRNA-1273 25 µg	Placebo	mRNA-1273 25 µg
	N=1007	N=3031	N=589	N=1911
Unsolicited AEs regardless of relationship to study vaccination				
All	512 (50.8)	1561 (51.5)	348 (59.1)	1022 (58.0)
Serious	2 (0.2)	9 (0.3)	1 (0.2)	15 (0.9)
Fatal	0	0	0	0
Medically attended	344 (34.2)	1002 (33.1)	242 (41.1)	678 (38.5)
Leading to discontinuation from study vaccine	0	0	1 (0.2)	1 (<0.1)
Leading to discontinuation from study	0	0	1 (0.2)	0
Severe	11 (1.1)	25 (0.8)	5 (0.8)	26 (1.5)
Non-serious	512 (50.8)	1558 (51.4)	348 (59.1)	1019 (57.9)
Severe	10 (1.0)	23 (0.8)	4 (0.7)	18 (1.0)
Special interest (AESI)	1 (<0.1)	5 (0.2)	1 (0.2)	4 (0.2)
MIS-C	0	0	0	0
Other	1 (<0.1)	5 (0.2)	1 (0.2)	4 (0.2)
Unsolicited AEs related to study vaccination				
All	82 (8.1)	290 (9.6)	72 (12.2)	298 (16.9)
Serious	0	0	0	2 (0.1)*
Fatal	0	0	0	0
Medically-attended	3 (0.3)	31 (1.0)	5 (0.8)	26 (1.5)
Leading to discontinuation from study vaccine	0	0	0	1 (<0.1)
Leading to discontinuation from study	0	0	0	0
Severe	8 (0.8)	19 (0.6)	3 (0.5)	14 (0.8)
Non-serious	82 (8.1)	290 (9.6)	72 (12.2)	298 (16.9)
Severe	8 (0.8)	19 (0.6)	3 (0.5)	13 (0.7)
Special interest (AESI)	1 (<0.1)	2 (<0.1)	0	2 (0.1)
MIS-C	0	0	0	0
Other	1 (<0.1)	2 (<0.1)	0	2 (0.1)

AE, adverse event; AESI, adverse event of special interest; MIS-C, multisystem inflammatory syndrome in children. An AE is defined as any event not present before exposure to study vaccination or any event already present that worsens in intensity or frequency after exposure. Percentages are based on the number of participants in the safety set. Solicited adverse reactions with toxicity grade = 0 that lasted beyond day 7 or started after day 7 are not included in this table. *Two participants reported SAEs considered related to study vaccination through the study including 1 SAE of pyrexia and febrile convulsion (SAE reported within 28 days, Tables S21 and S24); the other SAE considered related was new-onset Type 1 diabetes mellitus and diabetic ketoacidosis in a 1-year-old female reported 37 days post dose 2. This child has a significant family history of diabetes mellitus and a recent URI. Assessed as related, the Investigator also noted that the event is “more likely caused by a genetic predisposition to pre-diabetes and viral upper respiratory tract infection that occurred prior to second dose of study vaccine.
Data cut-off date: February 21, 2022.

Table S27. Observed Pseudovirus Neutralizing Antibody in Children 2−5 Years and 6−23 Months in Part 2 Per-Protocol Immunogenicity Subset

	2-5 years	6-23 months	18-25 years
	mRNA-1273 25 µg N=264	mRNA-1273 25 µg N=230	mRNA-1273 100 µg N=295
Baseline n*	264	230	294
GMC	7.7	7.9	11.1
(95% CI)‡	(7.2-8.2)	(7.4- 8.5)	(10.6-11.7)
Day 57, n*	264	230	291
GMC	1410.0	1780.7	1390.8
(95% CI)‡	(1272.0-1563.0)	(1616.2-1961.9)	(1263.5-1530.9)
GMFR§	183.3	225.3	125.8
(95% CI)‡	(164.0-204.9)	(200.4-253.3)	(113.0-140.0)
Seroresponse¶			
n/N1 (%)‖	261 (98.9)	230/230 (100)	289 (99.3)
(95% CI)††	(96.7-99.8)	(98.4-100.0)	(97.5-99.9)

CI, confidence interval; GMFR, geometric mean fold ratio; GMR, geometric mean ratio; GMC, geometric mean concentration; LLOQ, lower limit of quantification; LS, least-squares; N1, number of participants with non-missing data at baseline and the corresponding post-baseline time point; PsVNA, pseudovirus neutralizing antibody assay; ULOQ, upper limit of quantification. Neutralizing antibody titers assayed by PsVNA (ID_{50}). Log_{10} LLOQs is 10 and log_{10} ULOQ is 281600. Antibody values reported as below the LLOQ were replaced by 0.5 x LLOQ. Values greater than the upper limit of quantification ULOQ were replaced by the ULOQ if actual values were not available. Young adults included those 18-25 years of age in the mRNA-1273 group of the COVE study.

*Number of participants with non-missing data at the time point (baseline or postbaseline).

†95% CI calculated based on the t-distribution of the log-transformed values or the difference in the log-transformed values for GMC value and GMFR, respectively, then back transformed to the original scale for presentation.

§GMFR of S protein–specific binding antibody relative to day 1 on days 29 and 57.

¶Seroresponse at a participant level was defined as a change from below the LLOQ to equal or above 4 x LLOQ, or at least a 4-fold rise if baseline was equal to or above the LLOQ.

‖Number of participants meeting the criterion at the time point. Percentages are based on N1.

††95% CI is calculated using the Clopper-Pearson method. Data cut-off date: February 21, 2022.

Table S28. Secondary Efficacy Endpoints in Children 2−5 Years and 6−23 Months in Part 2 Per Protocol Efficacy Set

Endpoint, Per-protocol	Children 2 - 5 Years mRNA-1273 25 µg		Children 6 -23 months mRNA-1273 25 µg	
	Placebo N = 858	mRNA-1273 25 µg N = 2594	Placebo N = 513	mRNA-1273 25 µg N = 1511
Covid-19 (CDC definition)*				
Cases, n (%)	61 (7.1)	119 (4.6)	34 (6.6)	51 (3.4)
Incidence rate/1000 person-years (95% CI)†§	277.0 (211.9-355.8)	175.0 (145.0-209.4)	280.0 (194.0- 391.0)	138.2 (103.0-181.8)
VE % based on incidence rate (95% CI)¶	36.8 (12.5-54.0)		50.6 (21.4-68.6)	
Covid-19 (COVE definition) *				
Cases, n (%)	43 (5.0)	71 (2.7)	18 (3.5)	37 (2.4)
Incidence rate/1000 person-years (95% CI)†§	193.5 (140.1- 260.7)	103.8 (81.0- 131.0)	146.0 (86.6-230.8)	100.0 (70.4- 138.0)
VE % based on incidence rate (95% CI)¶	46.4 (19.8-63.8)		31.5 (-27.7-62.0)	
SARS-CoV-2 infection (regardless of symptoms)				
Cases, n (%)	93 (10.8)	198 (7.6)	45 (8.8)	81 (5.4)
Incidence rate/1000 person-years (95% CI)†§	433.4 (349.8- 531.0)	297.0 (257.0- 341.3)	374.4 (273.1- 501.0)	222.8 (177.0-, 277.0)
VE % based on incidence rate (95% CI)¶	31.5 (11.4-46.7)		40.5 (12.3-59.2)	
Asymptomatic SARS-CoV-2 infection				
Cases, n (%)	33 (3.8)	79 (3.0)	11 (2.1)	32 (2.1)
Incidence rate/1000 person-years (95% CI)†§	153.7 (105.8- 215.9)	118.5 (93.8- 147.6)	91.5 (45.7- 163.7)	88.0 (60.2- 124.2)
VE % based on incidence rate (95% CI)¶	22.9 (-19.5-49.3)		3.8 (-111.5-52.8)	

CDC, Centers for Disease Control and Prevention; CI, confidence interval; Covid-19, coronavirus disease 2019; mITT1, modified intent-to-treat; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2;
VE, vaccine efficacy.
*Covid-19 cases based on 1 symptom per CDC definition; Covid-19 primary case definition based on 2 symptoms used in the COVE trial.
†Person-years was defined as the total years from the randomization date to the date of event, last date of study participation, or efficacy data cut-off date, whichever was the earliest.
§Incidence rate is defined as the number of participants with an event divided by the number of participants at risk and adjusted by person-years (total time at risk) in each treatment group. The 95% CI is calculated using the exact method (Poisson distribution) and adjusted by person-years.
¶VE, defined as 1 - ratio of incidence rate (mRNA-1273 vs. placebo). The 95% CI of the ratio is calculated using the exact method conditional upon the total number of cases, adjusting for person-years. Data cut-off date: February 21, 2022.

Table S29. Secondary Efficacy Endpoints in Children 2−5 Years and 6−23 Months in Part 2 Modified Intent-To-Treat Set

Endpoint, mITT	Children 2 - 5 Years mRNA-1273 25 µg		Children 6 -23 months mRNA-1273 25 µg	
	Placebo N = 858	mRNA-1273 25 µg N = 2594	Placebo N =530	mRNA-1273 25 µg N = 1574
Covid-19 (CDC definition)				
Cases, n (%)	76 (8.6)	143 (5.4)	43 (8.4)	72 (4.7)
Incidence rate/1000 person-years (95% CI)†§	397.9 (313.5-498.0)	240.4 (202.6-283.2)	413.8 (299.4- 557.3)	224.2 (175.4- 282.3)
VE % based on incidence rate (95% CI)¶	39.6 (19.1-54.6)		45.8 (19.0-63.4)	
COVE case definition of Covid-19				
Cases, n (%)	53 (6.0)	90 (3.4)	24 (4.7)	53 (3.5)
Incidence rate/1000 person-years (95% CI)†§	274.3 (205.5-358.8)	150.2 (120.7-184.6)	227.2 (145.5- 338.0)	164.0 (122.8- 214.5)
VE % based on incidence rate (95% CI)¶	45.3 (21.6-61.4)		27.8 (-22.3-56.2)	
SARS-CoV-2 infection (regardless of symptoms)				
Cases, n (%)	125 (14.1)	257 (9.6)	58 (11.3)	120 (7.9)
Incidence rate/1000 person-years (95% CI)†§	675.9 (563.0- 805.3)	42.3 (390.0-499.9)	566.6 (430.2-732.5)	380.7 (315.7-455.3)
VE % based on incidence rate (95% CI)¶	34.6 (18.3-47.3)		32.8 (6.4.0-51.3)	
Asymptomatic SARS-CoV-2 infection				
Cases, n (%)	49 (5.5)	114 (4.3)	15 (2.9)	48 (3.2)
Incidence rate/1000 person-years (95% CI)†§	264.8 (196.0- 350.1)	96.2 (161.8- 235.7)	146.5 (82.0-241.6)	152.2 (112.2- 201.8)
VE % based on incidence rate (95% CI)¶	25.9 (-5.8-47.4)		-3.9 (-99.8-42.8)	

CDC, Centers for Disease Control and Prevention; CI, confidence interval; Covid-19, coronavirus disease 2019; mITT1, modified intent-to-treat; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2;
VE, vaccine efficacy.

*Covid-19 cases based on 1 symptom per CDC definition; Covid-19 primary case definition based on 2 symptoms used in the COVE trial.

†Person-years was defined as the total years from the randomization date to the date of event, last date of study participation, or efficacy data cut-off date, whichever was the earliest.

§Incidence rate is defined as the number of participants with an event divided by the number of participants at risk and adjusted by person-years (total time at risk) in each treatment group. The 95% CI is calculated using the exact method (Poisson distribution) and adjusted by person-years.

¶VE, defined as 1 - ratio of incidence rate (mRNA-1273 vs. placebo). The 95% CI of the ratio is calculated using the exact method conditional upon the total number of cases, adjusting for person-years. Data cut-off date: February 21, 2022.

Table S30. Sensitivity Analysis of Efficacy Against Symptomatic Covid-19

Endpoint, Per-protocol Set	Children 2 - 5 Years mRNA-1273 25 µg		Children 6 – 23 months mRNA-1273 25 µg	
	Placebo N = 858	mRNA-1273 25 µg N = 2594	Placebo N = 513	mRNA-1273 25 µg N = 1511
Covid-19 (CDC definition)*				
Cases, n (%)	81 (9.4)	179 (6.9)	52 (10.1)	74 (4.9)
Incidence rate/1000 person-years (95% CI)[†§]	371.4 (295.0-461.6)	265.5 (228.0-307.4)	433.9 (324.0-569.0)	201.6 (158.3-253.1)
VE % based on incidence rate (95% CI)[¶]	28.5 (5.9-45.3)		53.5 (32.4-67.8)	
COVE case definition of Covid-19*				
Cases, n (%)	55 (6.4)	106 (4.1)	30 (5.8)	51 (3.4)
Incidence rate/1000 person-years (95% CI)[†§]	248.9 (187.5-324.0)	155.6 (127.4-188.2)	245.7 (165.7-350.7)	138.2 (103.0-181.7)
VE % based on incidence rate (95% CI)[¶]	37.5 (11.8-55.3)		43.7 (8.5.0-64.8)	

CDC, Centers for Disease Control and Prevention; CI, confidence interval; Covid-19, coronavirus disease 2019; mITT1, modified intent-to-treat; SARS-CoV-2, severe acute respiratory syndrome coronavirus-2; VE, vaccine efficacy.

*Covid-19 cases based on CDC case definition) 1 systemic or 1 respiratory symptom + any positive Covid-19 test including home tests) and COVE case definition (2 systemic or 1 respiratory symptom + any positive Covid-19 test including home tests)

[†]Person-years was defined as the total years from the randomization date to the date of event, last date of study participation, or efficacy data cut-off date, whichever was the earliest.

[§]Incidence rate is defined as the number of participants with an event divided by the number of participants at risk and adjusted by person-years (total time at risk) in each treatment group. The 95% CI is calculated using the exact method (Poisson distribution) and adjusted by person-years.

[¶]VE, defined as 1 - ratio of incidence rate (mRNA-1273 vs. placebo). The 95% CI of the ratio is calculated using the exact method conditional upon the total number of cases, adjusting for person-years. Data cut-off date: February 21, 2022.

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